INTRODUCTION

We began studying the aromatic nitration of toluene in an effort to determine if there was a way to improve upon the regioselectivity of the nitrotoluene products. Conventional methods give very poor regioselectivity. Although several studies have been undertaken using zeolites, only one reports no meta-isomer in the product mixture. While studying the aromatic nitration, a side reaction was noted that appeared to produce an aliphatic nitration product by a very dissimilar means.

Aromatic Nitration

Nitration of aromatic compounds is a very important process for both industrial and academic purposes; of particular interest is the nitration of toluene. Nitrotoluene derivatives are used as precursors for not only explosives and propellants but also as the basis for urethanes and pharmaceutical intermediates.[1] The most desirable isomer of mononitrotoluene is *para*-nitrotoluene (4-nitrotoluene) because of the wide range of adaptability for further reaction (i.e. di-nitration and tri-nitration), although the *ortho*-isomer can be used for further nitrations as well. The conventional methods involve the use of nitric and sulfuric acids, both of which are very corrosive. Aromatic nitrations are selective with regard to the degree of nitration. For example, benzene is eight orders of magnitude more reactive than mononitrotoluene, which in turn is eight orders of magnitude more reactive than dinitrotoluene. This huge reactivity difference allows one to selectively mononitrate an aromatic ring without problems associated with over-nitration.

---

[1] Kwok, T.J.; Jayasuriya, K. *J. Org. Chem.* **1994**, *59*, 4939-4942.

However, this method is poorly regioselective, producing a mixture (ca. 57% *ortho-,* ca. 39% *para-,* and ca. 4% *meta-*) of mononitrotoluenes[2]. It also can produce oxidized alkyl side groups/chains resulting in unusable byproducts that are both costly to dispose of and environmentally detrimental.

To combat these problems, new methods for the nitration of aromatic compounds (e.g. toluene) have been introduced in recent years. The use of lanthanide triflates as catalysts offers a reduction in the acidity but requires chlorinated solvents and gives no appreciable improvement in regioselectivity.[3] Polysulfonic acid resins such as Nafion-H™ have been used to reduce the corrosive nature of the reaction but have not been able to provide any gains in regioselectivity nor increase of the *para-* isomer.[4]

The use of clays and zeolites for the nitration of toluene has been found to have distinct benefits over the conventional method as well as the other methods described. Laszlo, et al. developed a method using $Cu(NO_3)_2$ "claycop" on an acidic montmorillonite clay which selectively nitrates under Menke conditions (acetic anhydride as a coreagent).[5,6] This method gives a quantitative yield of mononitrotoluene with an *ortho-, meta-, para-* isomer distribution of 23:1:76, respectively. Laszlo, et al. suggests that the clay surface induces electronic stability favoring the *para-* isomer. This method does suffer from several disadvantages such as high dilution requirements, product isolation and inability to re-utilize the catalyst. Also, the excess acetic anhydride coreagent is difficult to remove and the stoichiometric use of the $Cu(NO_3)_2$ makes system

[2] Stock, L.M., "A Classic Mechanism for Aromatic Nitration". *Prog. Phys. Org. Chem.* **1976**, 12, 21-47.
[3] Waller, F.J.; Barret, A.G.M.; Braddock, D.C.; Ramprasad, D. *Chem. Comm.* **1997**, 613.
[4] Olah, G.A.; Malhotra, R.; Narang, S.C. *J. Org. Chem.* **1978**, *43*, 4628.
[5] DeLaude, L.; Laszlo, P.; Smith, K. *Acc. Chem. Res.* **1998**, *26*, 607.
[6] (a)Laszlo, P. *Acc. Chem. Res.* **1986**, *19*, 121 (b)Laszlo, P.; Vandormael, J. *Chem.Lett.* **1988**, 1843. (c)Cornelis, A.; DeLaude, L.; Gerstmans, A.; Laszlo, P. *Tetrahedron Lett.* **1988**, *29*, 5657

regeneration difficult on an industrial scale.[1] Another method employing clays has been introduced by Smith, et al., in which a large port mordenite clay and benzoyl nitrate is used. This process affords 60% *para*-isomer selectivity. This method does suffer from the sensitivity of the benzoyl nitrate to decomposition as well as handling issues arising from the instability of benzoyl nitrate.[7]

The most promising of the new methods are those making use of zeolites. A higher degree of regioselectivity arises in part from the pore size of the zeolite. The zeolites used are, molecular sieves, allowing only molecules of a particular size and smaller to pass through. The zeolite used during this research is H-ZSM-5, which is composed of a series of 5-membered oxygen-containing rings. It can be synthesized by using organic molecules such as tetrapropylammonium bromide as directing agents. When the zeolites are crystallized from solution, the organic molecules are then incorporated into the zeolite crystals filling the intracrystalline void spaces. While in the spaces, the organic molecules may be in the form of either cations or occluded salt molecules. This particular catalyst is somewhat different from other zeolites in that it has a uniform pore structure and does not have the supercages common to other zeolites. This allows the H-ZSM-5 to avoid the bottlenecking that can occur at the window entrances of the supercages. The absence of this bottlenecking also allows the H-ZSM-5 to avoid coking problems, because the uniform pore size will not allow the large polynuclear hydrocarbons responsible for coking, access to the zeolite structure.[8]

---

[1] Kwok, T.J.; Jayasuriya, K. *J. Org. Chem.* **1994**, *59*, 4939-4942.
[7] Smith, K.;Fry, K; Butters, M.; Nay, B. *Tetrahedron Lett.* **1989**, *30*, 5333.
[8] Chen, N.Y., et. al. "Molecular transport and reaction in zeolites: design and application of shape selective catalysts." 1994. 15.

The H-ZSM-5 is composed of SiO_2 and Al_2O_3, and has an elliptical pore size of 5.1-5.6 Å. This pore size will allow the cylindrical toluene molecule to move through its channels (pores).[9] During the nitration process, the *nitro-* group is preferentially substituted at the *para-* position because the pore size will allow the substitution. The physical size of the zeolite pore (5.1-5.6 Å) will inhibit the formation of *ortho-* and *meta-* nitrotoluenes because these isomers are somewhat larger than the pore; measuring approximately 6.7 Å.

It has been suggested that by increasing the SiO_2 to Al_2O_3 molar ratio (SAR) within the zeolite structure, the regioselectivity can be markedly increased. Using an SAR of 30, the ortho: meta: para (o:m:p) ratio was 32:1:67 while increasing the SAR to 80 gave an o:m:p ratio of 29:1:70.[10] This trend has been shown to continue up to an SAR of 1000 where the o:m:p ratio is 5:0:95.[10]

In the course of ours studies, we found a side product, which occurred from aliphatic nitration. We became interested in the aliphatic nitration product because this product had not been isolated using this method previously. The difficulty in producing nitrated aliphatic compounds also piqued our interest since many nitrated aliphatics are used industrially and are expensive to synthesize using existing methods.

Aliphatic Nitrations

As with the nitrated aromatics, nitrated aliphatics are both academically and industrially important. While the nitrated aliphatics are important, they are not as easy to synthesize as their aromatic cousins. This difficulty stems from the generally non-acidic

[9] Kucherov, A.V; Slinkin, A.A.; et al. *Catal. Lett.* **1988**, *1*, 311.
[10] Jayasuriya, K. U.S Patent 5 946 638, 1999.
[10] ibid.

nature of the protons attached to the aliphatic carbons. Unlike aromatic compounds, such as toluene, aliphatic compounds do not posses the π-electron density needed for electrophilic substitution. Without this property, the aliphatics must generally rely upon the acidity of the protons that are attached to the carbons of the aliphatic system. Unfortunately, these protons are not very acidic, which reduces the reactivity of the aliphatic system. In order to overcome the lack of proton acidity, reactions to nitrate aliphatic systems have been carried out under basic conditions. The bases that are employed are strong enough to remove protons from the aliphatic system allowing for the nitration to take place. This type of reaction has a distinct drawback in that the presence of strong bases can damage or destroy compounds that have base sensitive components.

Although there are some problems associated with the nitration of aliphatic systems, nitrated aliphatics have been produced for many years using several different methods. Typical aliphatic nitrations include but are not limited to the following methods; gas phase nitration of alkanes and S_N2 displacement of alkyl halides by nitro groups.

Gas phase nitration of alkanes is the most common industrial method of producing nitroparaffins[11] as these are simple nitrated aliphatics. This nitration process is accomplished at high temperature, typically 400º C, and involves a free radical mechanism. While this reaction is effective at producing nitrated aliphatics it does have several drawbacks, the biggest being the very harsh conditions under which the reaction takes place. The high temperatures may not have detrimental effects on simple alkanes but on more complex molecules the temperatures needed to initiate the radical addition

[11] Kirk-Othmer Encyclopedia of Chemical Technology. John Wiley & Sons, Inc. New York. 1996. p 204.

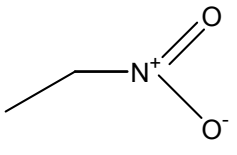
could be destructive to the point of uselessness. Also this type of reaction produces many oxidation side products[12] that may prove difficult to remove.

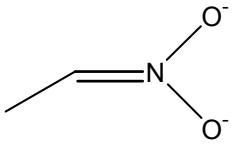
The nitroparaffins that are most commonly produced using gas phase nitration have a number of uses. Currently, four nitroparaffins are generally available commercially: nitromethane, nitroethane, 1-nitropropane, and 2-nitropropane. Nitroparaffins are produced when the nitro group attaches to a carbon in the aliphatic system through its nitrogen, while an isomer of nitroparaffins, alkyl nitrite, is produced when the nitro group attaches to a carbon of the aliphatic system through one of its oxygen atoms. Although the four nitroparaffins are the most common, other more complex nitroparaffins and polynitroparaffins are also available. Nitroparaffins are considered excellent solvents for coating materials, waxes, resins, gums and dyes.[13] Nitroparaffins can undergo aldol-type reactions with aldehydes and ketones to produce nitro alcohols.[14] Nitroparaffins can be readily reduced using a variety of methods from iron and hydrochloric acid to high-pressure hydrogenation over Raney nickel.[15]

Beyond the great utility of nitroparaffins, perhaps the most important use for nitroaliphatics is their use in synthetic methods. Nitro compounds can be used to insert carbonyl functionality to existing aliphatic systems using the Nef reaction. The Nef reaction is considered the most important type of transformation dealing with nitro compounds.[16] This transformation can be used to convert primary and secondary nitro compounds into aldehydes or ketones. The methods for the transformation include

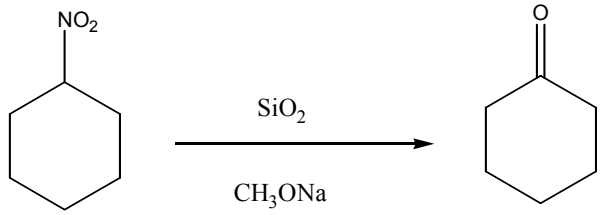
[12] The Nitro Group in Organic Synthesis. Ono, N. Wiley-VCH. New York, 2001. pp. 7.
[13] Kirk-Othmer Encyclopedia of Chemical Technology. John Wiley & Sons, Inc. New York. 1996. pp 205-207.
[14] Troops, E.E., Jr. *J. Phys. Chem.* **60**, 304 (1956)
[15] Ioffe, S.L., Tartakovskii, V.A., and Novikov, S.S. *Russ. Chem. Rev.* **35**, 19 (1966).
[16] The Nitro Group in Organic Synthesis. Ono, N. Wiley-VCH. New York, 2001. pp. 159.

treatment of nitronates with acid, oxidation of nitronates, and reduction of nitroalkenes. Nitronate is the anion form of an aliphatic nitro compound, whereas a nitro compound is a neutral species. Shown below is an example of a nitro compound, nitroethane (A), and its nitronate analogue, ethyl nitronate (B).


(A)


(B)

The classical procedure in a Nef reaction transformation is carried out using acid treatment, normally with a strong acid such as aqueous HCl. However, the use of base followed by acid is incompatible with many polyfunctional substrates, in addition to the possible side reactions. [17,18,19] Due to these problems, modifications have been made in which silica gel is used as an acid during the Nef transformation. Shown below is a convenient method for transforming nitrocyclohexane into cyclohexanone;

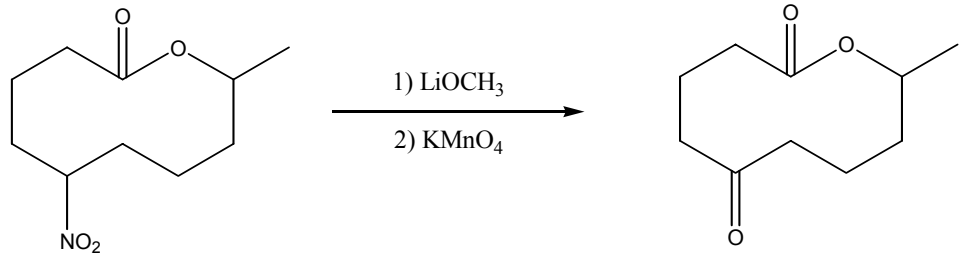


(1)[20]

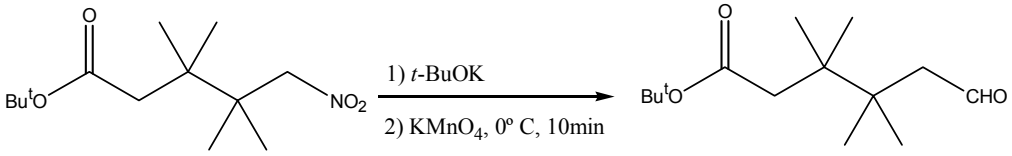
In general, most Nef transformations of this type are carried out in either water or water containing solvents.

[17] Noland, W.E., **55**, 137, (1995)
[18] Neilsen, A.T., *The Chemistry of Functional Groups; Nitrones, Nitronates, and Nitroxides*, ed. by S. Patai and Z. Rappoport, John Wiley, London, 1989.
[19] Pinnick, H.W. In *Organic Reacitons*, ed. by L.A. Paquette, John Wiley, **38**, Chapter 3 (1990).
[20] The Nitro Group in Organic Synthesis. Ono, N. Wiley-VCH. New York, 2001. pp. 160.

The oxidative method uses a variety of oxidizing agents, such as but not limited to the following, for the oxidation of nitro compounds to aldehydes and ketones: potassium permanganate[21], hydrogen peroxide[22], ozone[23] and sodium chlorite[24]. Potassium permanganate provides a simple and effective method of converting various nitro compounds with 80-96% yields. This oxidizer can also produce quaternary aldehydes despite their instability.[25] Shown below are two common preparations of a ketone (2a) and an aldehyde (2b) using the potassium permanganate oxidizer;



(2a)[25]

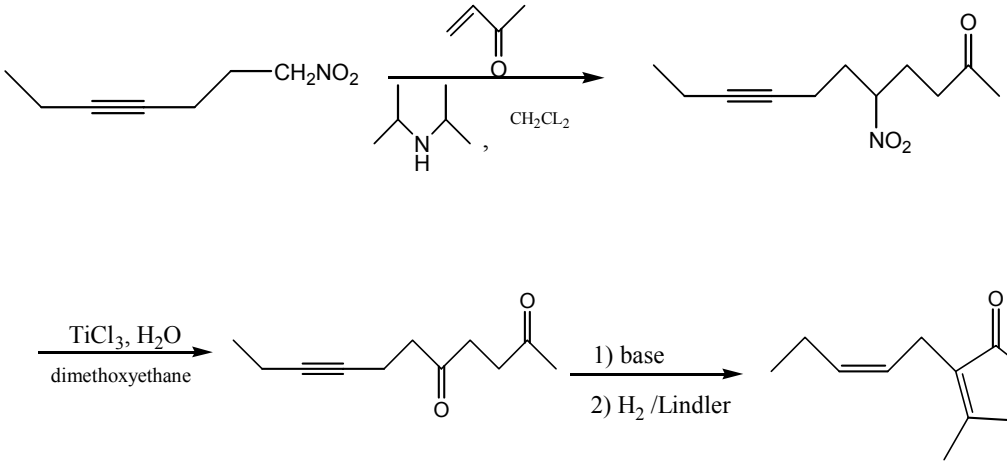


(2b)[25]

Reduction of nitroalkenes is also an effective route for the Nef transformation and can be carried out using a variety of reducing agents. For example, aqueous titanium (III) chloride can be used to reduce nitro compounds to imines that are readily hydrolyzed into

[21] Shechter, H., and Williams,F.T. *J. Org. Chem* .**27,** 369 (1962)
[22] Olah, G.A., Aravananaghi, M., Vankar, Y.D., Prakash, G.K.S. *Synthesis*, 662 (1980).
[23] McMurry, J.E., Melton, J., Padgett, H. *J. Org. Chem.* **39**, 259 (1974); *Org. Synth*. **6**, 648 (1988).
[24] Ballini, E., Petrini, M. *Tetrahedron Lett*., **30**, 5329 (1989).
[25] The Nitro Group in Organic Synthesis. Ono, N. Wiley-VCH. New York, 2001. pp. 161.

carbonyl compounds.[26] Using the Michael addition of nitroalkanes to enones followed by the reaction of titanium (III) chloride provides an excellent route to 1,4-diketones and further reaction can prepare cyclopentenones. Shown below is an example of using a reducing agent and the Michael addition to produce *cis*-jasmone, which occurs naturally in the flowers of the Jasmine plant (*Jasminum officinale*) and has a variety of uses including therapeutic oils and body lotions.



(3)

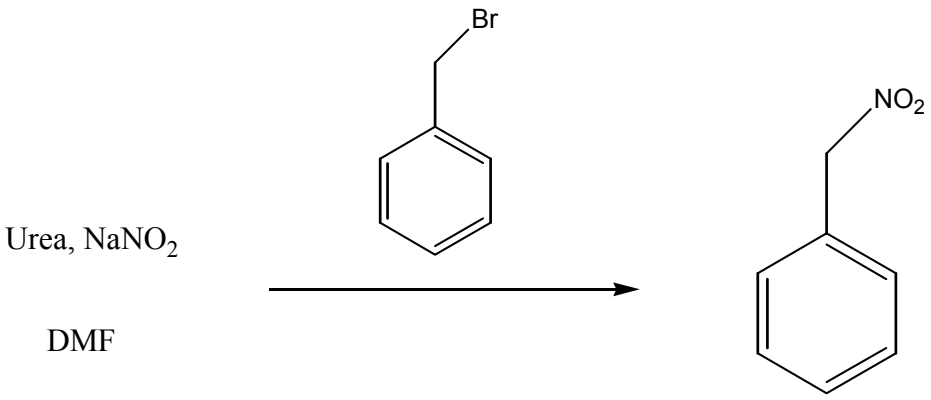
The use of titanium (III) chloride does present some problems as it is very acidic and as such, acid-sensitive compounds will not survive this treatment. If these acid-sensitive compounds are present, sodium acetate or ammonium acetate is added to the reaction to moderate the pH levels at 5-6.[27]

These have been just a few examples of how the Nef reaction can be used to transform nitro compounds into aldehydes and ketones. The ability to make direct conversions from nitro compounds to ketones is an important tool and is especially important for the preparation of arylacetones.[28]

[26] McMurry, J.E., Melton, J. *J. Am. Chem. Soc.* **93**, 5309 (1971).
[27] McMurry, J.E., Melton, J. *J. Org. Chem.*, **38**, 4367 (1973).
[28] The Nitro Group in Organic Synthesis. Ono, N. Wiley-VCH. New York, 2001. pp. 165.

The uses for nitrated aliphatics are many and varied but the actual preparation of the nitrated aliphatics has been a problem in the past. Simple nitroparaffins can be produced as outlined above but production of more complex nitro compounds has proven to be difficult. As stated earlier, there are many ways to produce nitrated aliphatics but the more complex compounds require complicated and time consuming synthetic processes.

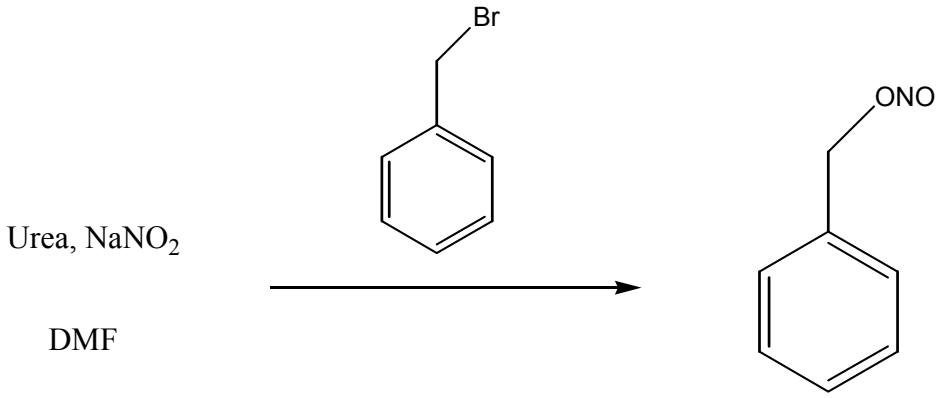
One method for producing nitrated aliphatics that can be applied to molecules that are more complex is the Kornblum reaction[29], which is an S_N2 displacement of an alkyl halide by a nitro group. While this reaction does produce phenylnitromethane, the yields are relatively low and it suffers from the fact that an alkyl halide must be substituted in the aliphatic system to be effective. Phenylnitromethane was seen as an important product from the zeolite reactions since it had previously only been produced in significant quantities using a selected few reaction types that required expensive feed stock materials and involved synthetic procedures. Shown below is the general form of a Kornblum reaction;



(4a)

[29] Kornblum, N., Weaver, W., *J. Am. Chem. Soc.* **80**, 4333 (1958)

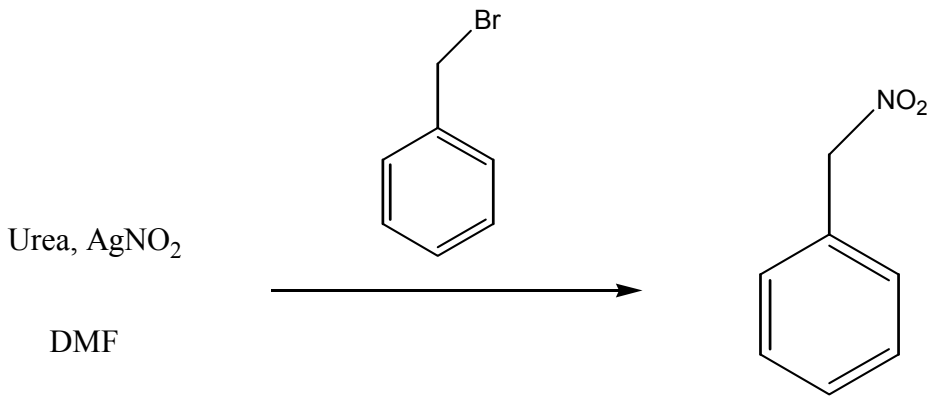
The Kornblum reaction produces not only nitro compounds (4a) but also produces nitrite esters[30] (4b).



(4b)

The nitrite esters are formed when the carbon of the aliphatic system attaches to oxygen of the nitro group. This is caused by the ambident nucleophilicity of the sodium ion[31]. Ambident nucleophilicity refers to the ability of the nitronate anions to attack from either the carbon, a soft nucleophile, or the oxygen, a hard nucleophile. These will attack soft and hard electrophiles, respectively[32]. The nitrite esters produced are usually considered an impurity and must be removed before successive synthetic processes can be undertaken. To eliminate the nitrite ester production, the Victor Meyer[33] reaction can be used with silver nitrite. This form of the Victor Meyer reaction does not produce the nitrite esters because the silver ion does not possess the ambient nucleophilicity that the sodium ion does. A general form of the Victor Meyer reaction is shown below:

[30] Vollhardt, K., Schore, N. Organic Chemistry: Structure and Function. 4th ed. W.H. Freeman and Company, New York, 2003. pp. 771.
[31] ibid.
[32] ibid
[33] V. Meyer, Ann. 1874, 171, p. 1 et seq.



(5)

Even though the Victor Meyer reaction does not produce the nitrite esters, an alkyl halide must be present in aliphatic system for the reaction to be effective. The Victor Meyer reaction can produce phenylnitromethane but it does so in much the same manner of the Kornblum reaction, both requiring relatively cold reaction temperatures (≈ -15° C) to be effective.

There are several methods reported for the synthesis of phenylnitromethane, but none of them are both convenient and reliable. The preparation of phenylnitromethane is reported in *Organic* Synthesis from sodium phenylnitroacetonitrile, which is synthesized using metallic sodium in ethyl alcohol. From this solution, sodium ethoxide precipitates to which is added benzyl cyanide and methyl nitrate. The phenylnitromethane is then produced from the resulting sodium phenylnitroacetonitrile using a boiling alkaline solution of water and sodium hydroxide. The mixture must then be cooled to –5º C and acidified. After organic and aqueous extractions, phenylnitromethane is isolated, giving yields of approximately 50% based on the benzyl cyanide. While this method will produce phenylnitromethane, it does involve the use of not only difficult to handle, but dangerous substances. Benzyl cyanide is very toxic, and the methyl nitrate used for this reaction must be produced in the laboratory, as it is not currently commercially available.

Methyl nitrate also poses safety concerns because it self oxidizes, which means it does not need an external source of oxygen to combust. Sodium metal must be handled carefully to avoid exposure to water. This method also requires several days of isomerization once the initial synthesis is completed.

Some other methods of producing phenylnitromethane involve the interaction of benzendiazonium chloride and nitromethane in alkaline solution[34]; the action of silver nitrite on benzoyl chloride[35] or iodide[36]; and the condensation of ethyl nitrate with benzyl cyanide and subsequent hydrolysis.[37] These methods also suffer from both difficult syntheses and the use of dangerous reactants. Another method involves a mixture of benzoyl alcohol, dichloromethane, sodium nitrite, and acetic acid. Concentrated HCl was added and the mixture was left to sit overnight. This method was reported to produce yields of 80%[38] but did not perform as reported in laboratory testing. Makosza, et al.[39] later refuted this method as erroneous. While there are many needs and uses for aliphatic nitro compounds, their synthesis is often difficult and can involve many steps with hazardous reagents.

[34] Bamberger, Schmidt, and Levinson, ibid. **33**, 2053 (1900).
[35] Hollemann, Rec. trav. Chim. **13**, 403 (1894).
[36] Hantzsch, and Schultze, Ber. **29**, 700 (1896).
[37] Wislicenus and Endres, ibid. **35**, 1755 (1902); cf. Gatterman-Weiland, "Laboratory Methods of Organic Chemistry," p. 256. Translated from the twenty-fourth German edition by W. McCartney, the MacMillan Company, New York, 1937.
[38] Baruah, A., Kalita, B., Barua, C. *Synlett*. **7**, 1064-1065 (2000).
[39] Makosza, M., Barbasiewicz, M., Wojciechowski, K. *Synlett.* **2001**, 7, 1121-1122.

EXPERIMENTAL

General

Toluene and DMF were HPLC grade; nitric acid (90%), decane, chloroform, diethyl ether, urea, sodium nitrite, and benzyl bromide were reagent grade. Nitric acid, chloroform and diethyl ether were purchased from Fisher Scientific; decane was purchased from Sigma Chemical Company; urea was purchased from Aldrich Chemical; sodium nitrite was purchased from Mallinckrodt, and benzyl bromide was purchased from Avocado Chemical through Fisher Scientific. Toluene and DMF were purchased from Burdick & Jackson. Ethyl benzene and 2,4-dichlorotoluene were purchased from Acros Chemical through Fisher Scientific. Toluene, decane, chloroform, diethyl ether, benzyl bromide, urea, sodium nitrite and DMF were used without further purification. Nitric acid was purified using urea with air sparging.[40] Zeolite was obtained from the Zeolyst Corporation and Tricat Zeolites and calcined overnight at 550º C and stored at 130º C until use. Reactions were followed using an HP6890 series gas chromatograph equipped with an HP5 column and an FID detector. Decane was used as an internal standard for analysis.

GC Analysis Method

The analyses of the fractions taken from the nitration reactions were performed using an HP 6890 Gas Chromatograph with auto-sampler. The capillary column used was an HP-5, cross-linked 5% phenyl methyl siloxane. Column dimensions are as follows; 30m x 0.32mm with a film thickness of 0.25μm. A helium gas split ratio of 100:1, a split flow of 200mL/min and a column flow rate of 2.00mL/min were used. A

---

[40] Freeman, P., Shepard, I.G. *Org. Syn.,* **43**, 84 (1963).

temperature program was set up to aid in peak separation and is as follows: initial temperature 125° C held for two minutes, temperature ramp at two minutes to 200° C @ 20° C/min. Final temperature was held at 200º C for one minute. Total analysis time was 6.75 minutes. It was determined that an injection volume of 1µL was sufficient. Integration was set to begin at 1.80 minutes to remove the solvent peak from the chromatogram.

General reaction for ring nitration. (JB-1-121)

To a 125mL, 4-neck, round bottom flask equipped with an overhead stirrer, condenser, thermometer, sparger, and heating mantle, were charged 80mL of toluene, 0.8mL of decane and 20.05g of zeolite. This mixture was heated to a reaction temperature of 80-85º C with stirring and nitrogen sparging. At reaction temperature, 1.75mL of purified 90% nitric acid was added. Reaction was allowed to proceed for one hour with continued stirring and sparging. Each sample is prepared for analysis by gas chromatograph in the following manner; using a standard autosampler vial, 0.5mL of toluene, 0.5mL of DI water and 0.5mL of sample are mixed. The vial is then sonicated for one (1) minute. The vial is then centrifuged for two (2) minutes.

Analysis indicated total nitrotoluene (aromatic mononitration products) to be 79.8% by area based on the internal standard with isomeric distribution being; 21.1% ortho-nitrotoluene, 1.34% meta-nitrotoluene and 77.5% para-nitrotoluene. (See Fig. 1)

General reaction for the pre-treatment ring nitration. (JB-2-5)

To a 125mL, 4-neck, round bottom flask equipped with an overhead stirrer, condenser, thermometer, sparger, and heating mantle, were charged 60mL of chloroform

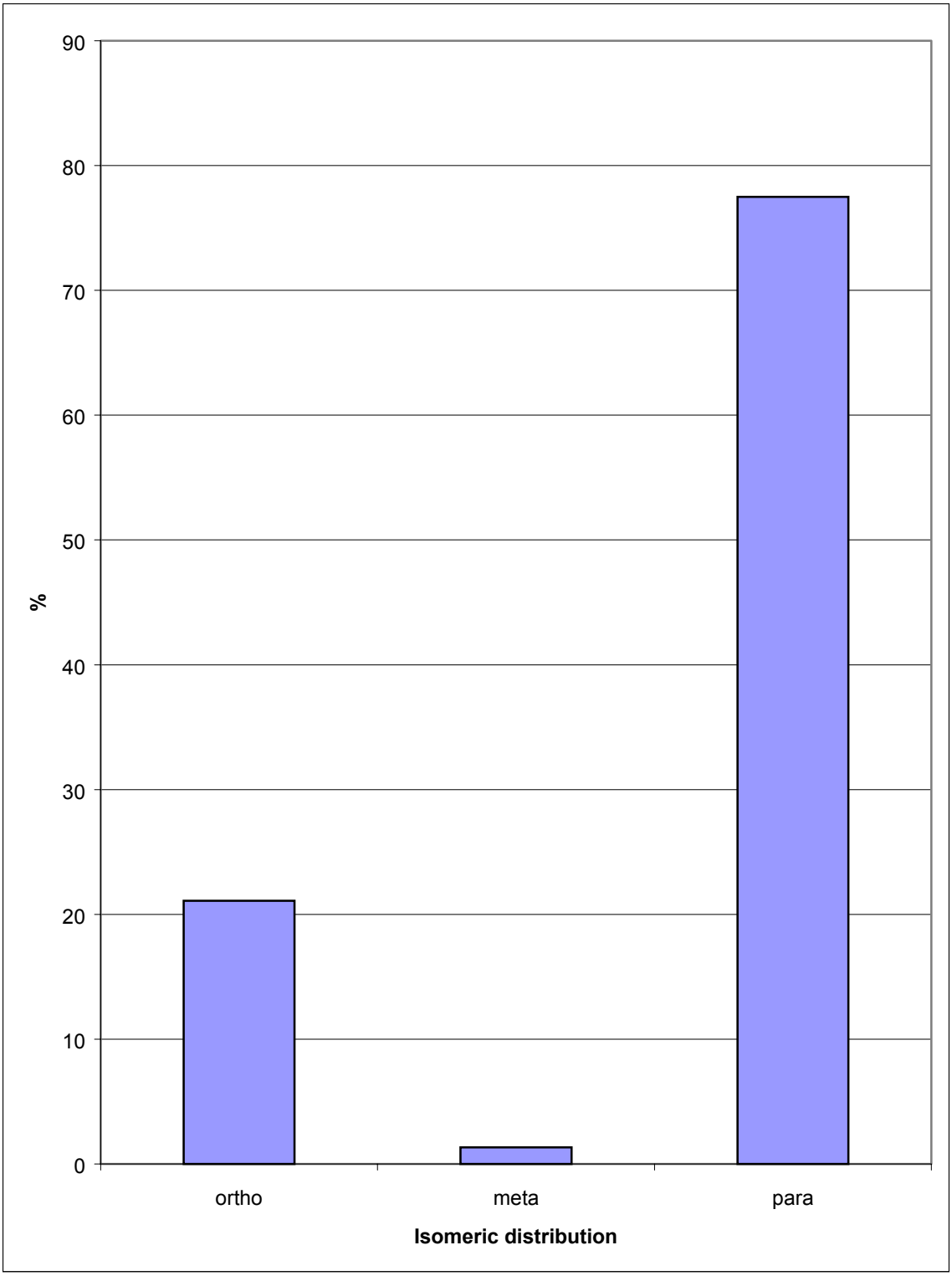


Figure 1: Isomeric distribution of a typical zeolite nitration reaction.

and 15.10g of zeolite. This mixture was heated to the pretreatment temperature of 50-55º C with stirring and nitrogen sparging. At pretreatment temperature, 1.30mL of purified 90% nitric acid was added. The mixture was allowed to stir for one hour. To the mixture, 60mL of toluene was added while increasing the temperature to the reaction temperature of 80-85º C with continued stirring and sparging. Reaction was allowed to proceed for two hours with stirring and sparging.

After two hours, the mixture was allowed to cool to room temperature. The reaction mixture was vacuum filtered using a Büchner funnel with #5 ashless filter circles. Filtrate was concentrated by rotary evaporation to afford 0.73g of light orange oil, analyzed by GC to have 77.0% by area *p*-nitrotoluene. (See Fig. 2)

General reaction for the production of phenylnitromethane. (JB-2-37)

To a 125mL, 3-neck, round bottom flask equipped with an overhead stirrer, thermometer, condenser, and heating mantle, were charged 50mL of toluene and 25.10g of zeolite. This mixture was heated to a reaction temperature of 80-85° C with stirring. At reaction temperature, 2.3mL of 90% nitric acid were added. Reaction was allowed to proceed for at least two hours with continued stirring.

After two hours, the mixture was allowed to cool to room temperature. The reaction mixture was vacuum filtered using a Büchner funnel with #5 Whatman ashless filter circles, and washed with toluene (3 x 50mL). The filter cake was allowed to dry under vacuum; and then transferred to a 150mL beaker. To this beaker, 50mL of toluene were added; the beaker was then placed in a sonicator (FS-30) for five minutes to ensure

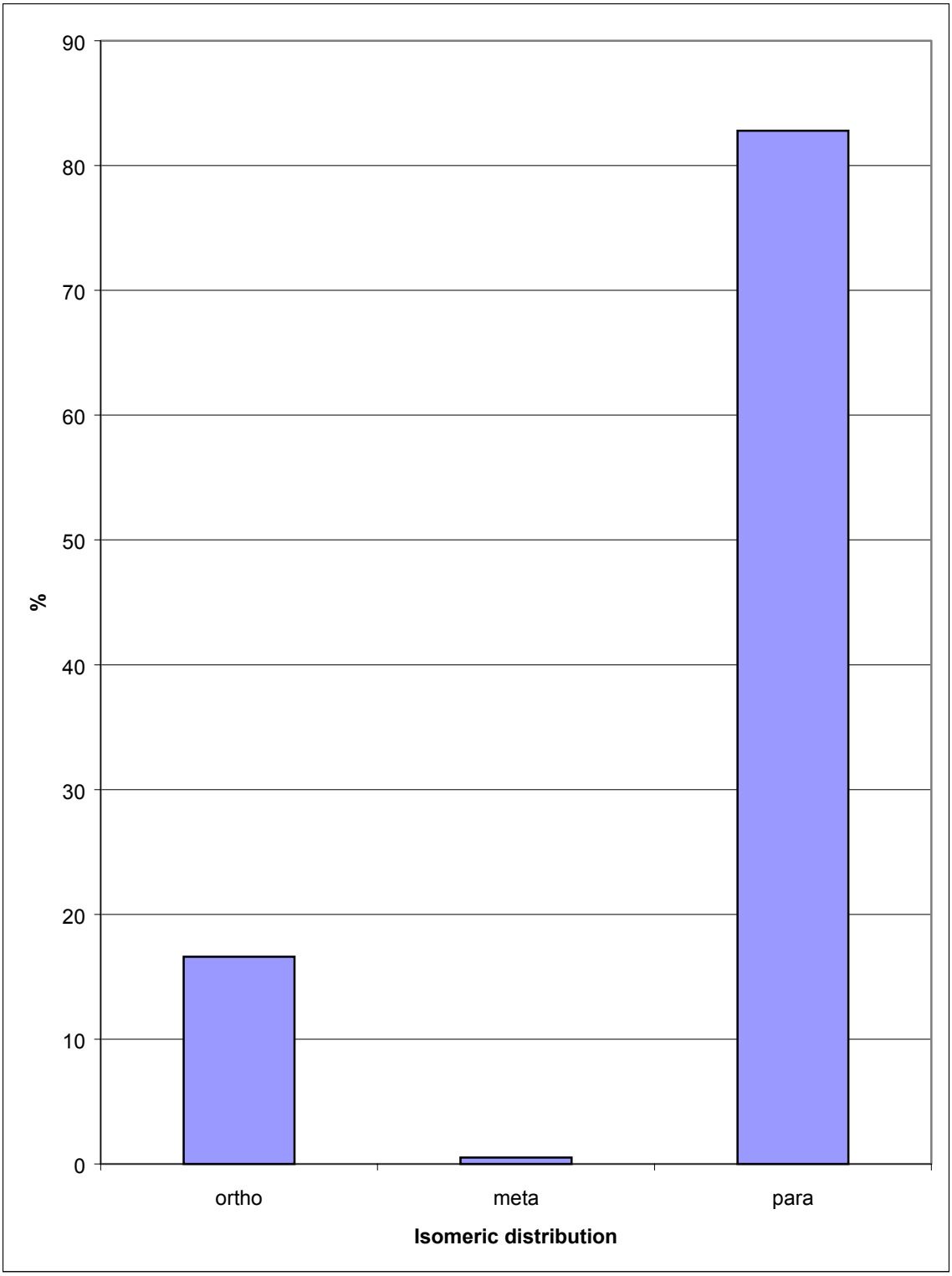


Figure 2: Isomeric distribution of a typical chloroform pretreatment nitration reaction.

product removal from the zeolite channels. The filter cake was again filtered under vacuum and washed with toluene (1 x 50mL). The combined filtrates were concentrated by rotary evaporation to afford 2.53g of light yellow oil, analyzed by GC to have 40.8% by area phenylnitromethane. (See Fig. 3)

The oil was further purified by dissolving in 20mL of organic solvent (dichloromethane) and extracting with 50% NaOH(aq). The aqueous layer was acidified, extracted with 20 mL dichloromethane and the organic layer washed five times with 10mL 10% $NaHCO_3$ (aq) and concentrated by rotary evaporation to afford 0.71g viscous light orange oil 67.7% by area PNM.

General reaction for the production of high purity phenylnitromethane.

To a 1000mL, 3-neck, round bottom flask equipped with and overhead stirrer, thermometer, condenser, and heating mantle, were charged 300mL of toluene and 25.2g of zeolite (280 SAR). This mixture was heated to a reaction temperature of 80-85° C with stirring. At reaction temperature, 50mL of unpurified 90% nitric acid were added. Reaction was allowed to proceed at least three hours with continued stirring.

After three hours, the mixture was allowed to cool to room temperature. The reaction mixture was vacuum filtered using a Büchner funnel with #5 Whatman ashless filter circles and washed with toluene (3 x 50mL). The filter cake was allowed to dry under vacuumand then it was transferred to a 150mL beaker. To this beaker, 50 mL of toluene were added. The beaker was then placed in a sonicator (FS-30) for five minutes to ensure product removal from the zeolite channels. The filter cake was again filtered under vacuum and washed with toluene (1 x 50mL). The combined filtrates were

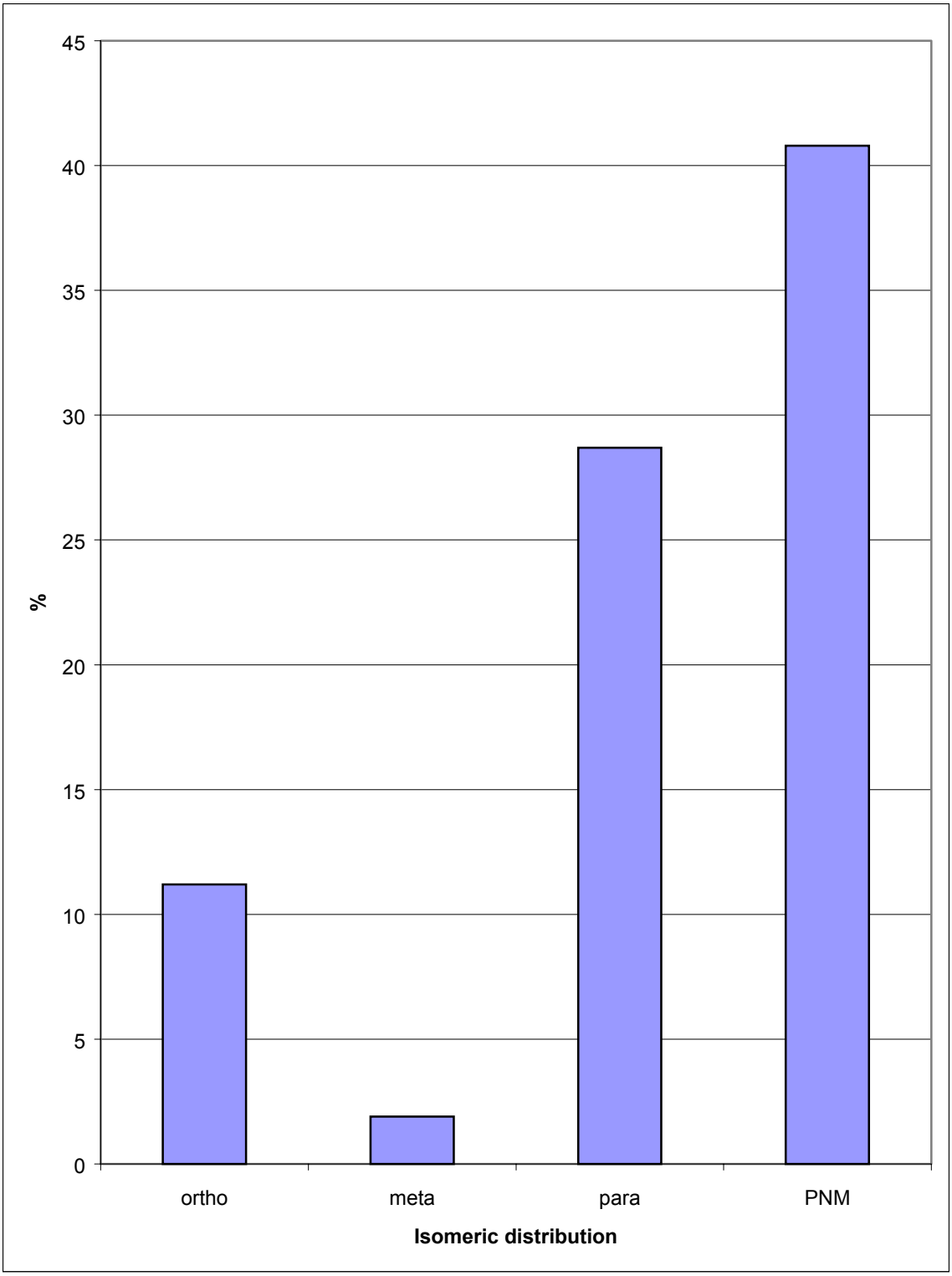


Figure 3: Product distribution for a typical reaction to produce phenylnitromethane.

concentrated by rotary evaporation to afford 90.75g of light yellow oil analyzed by GC to have 13.6% by area of phenylnitromethane.

The oil was purified by dissolving in 100mL of organic solvent (dichloromethane) and extracting with 50% NaOH (aq). The aqueous phase was removed and acidified, extracted with 200mL of dichloromethane and the organic phase was washed with $NaHCO_3$ (sat) (2 x 50mL), dried over Na_2SO_4 and concentrated by rotary evaporation to afford 15.93g of light yellow oil 71.4% by area PNM.

Product oil was further purified by reduced pressure fractional distillation to yield 3.01g of light yellow oil 91.6% by area phenylnitromethane. (See Fig. 4) ^1H NMR ($CDCl_3$) δ 5.41 (s, benzylic, 2H), 7.42 (s, ArH's, 5H); IR (neat) υ_{max}/cm^{-1} 1375, 1534 (two C-NO_2), 2915 (C-H), 3036, 3067 (two Ar C-H)

Kornblum method for production of phenylnitromethane (JB-2-61)

The procedure used was adapted from Kornblum and Weaver. To a 300mL, 3-neck, round bottom flask equipped with a magnetic stirrer, thermometer, condenser and cooling bath were charged with 12.07g of urea, 10.58g of sodium nitrite, and 150mL of DMF. This mixture was cooled to a reaction temperature of –15º to –20º C using a bath of dry ice in acetone and 1-octanol with stirring.

After cooling, 17.1g (11.8mL) of benzyl bromide were added. The reaction was allowed to proceed for three hours under a nitrogen sweep with continued stirring and cooling.

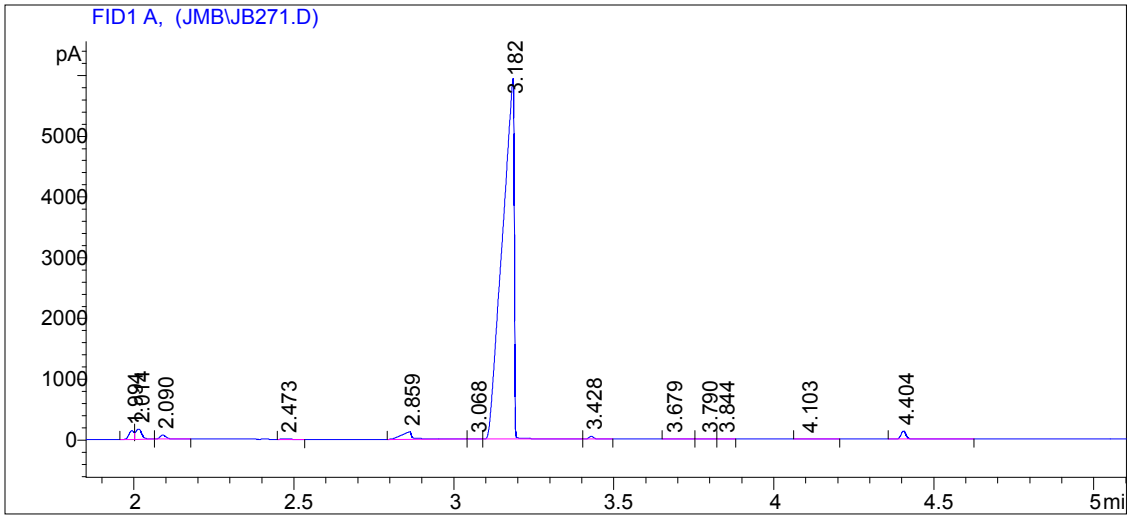


Figure 4: GC chromatogram showing product of the high purity phenylnitromethane reaction, JB-2-71

The cold solution was poured into 800mL of ice water. The water was extracted using toluene (50mL x 2) and diethyl ether (50mL x 4). Extracts were combined and concentrated by rotoevaporation, affording 18.76g of product. Concentrated product was purified using reduced pressure distillation yielding 3.73g of 92.1%, by area of phenylnitromethane. (See Fig. 5) ^{1}H NMR ($CDCl_3$) δ 5.41 (s, benzylic, 2H), 7.42 (s, ArH's, 5H); IR (neat) υ_{max}/cm^{-1} 1375, 1534 (two C-NO_2), 2917 (C-H), 3036, 3067 (two Ar C-H)

General reaction for the production of 2,4-dichlorophenylnitromethane.

To a 125mL, 3-neck, round bottom flask equipped with a magnetic stirrer, thermometer, condenser, and heating mantle, were charged 75mL of 2,4-dichlorotoluene and 15.35.g of zeolite. This mixture was heated to a reaction temperature of 80-85° C with stirring. At reaction temperature, 10.4mL of 90% nitric acid were added. Reaction was allowed to proceed for at least three hours with continued stirring.

After three hours, the mixture was allowed to cool to room temperature. The reaction mixture was vacuum filtered using a Büchner funnel with #5 Whatman ashless filter circles, and washed with dichloromethane (2 x 10mL).

The reaction mixture was extracted using 50% NaOH, aqueous phase was removed and acidified. The acidified mixture was vacuum filtered using a Büchner funnel with #5 Whatman ashless filter circles, the filter cake was allowed to dry under vacuum, yielding 1.3g of 86.1% DCPNM by GC. Product was further purified using a 20% $NaHCO_3$ extraction; solid was further purified under reduced pressure producing 0.95g of light yellow solid 95.2% by area dichlorophenylnitromethane. (See Fig. 6)

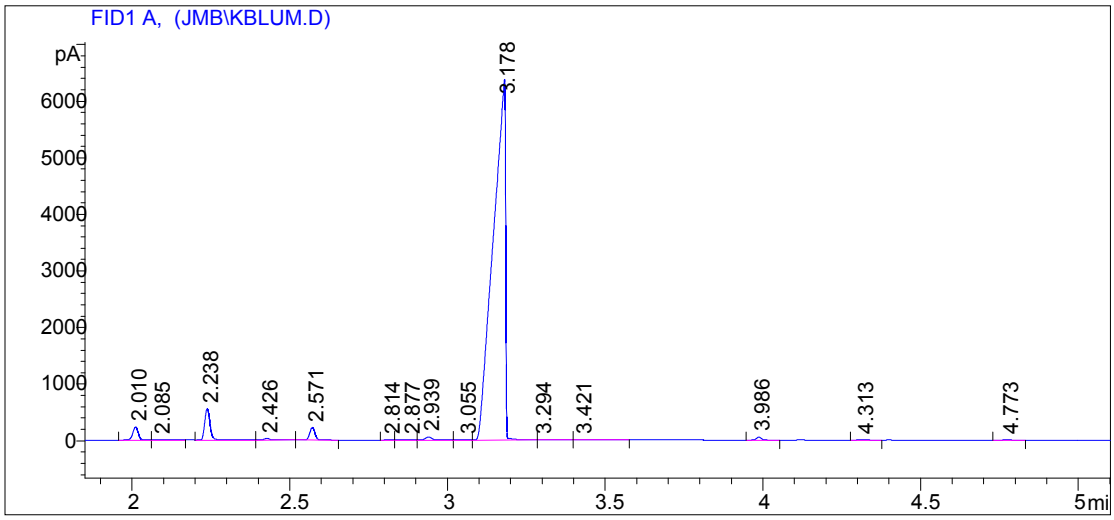


Figure 5: GC chromatogram showing product of the Kornblum reaction

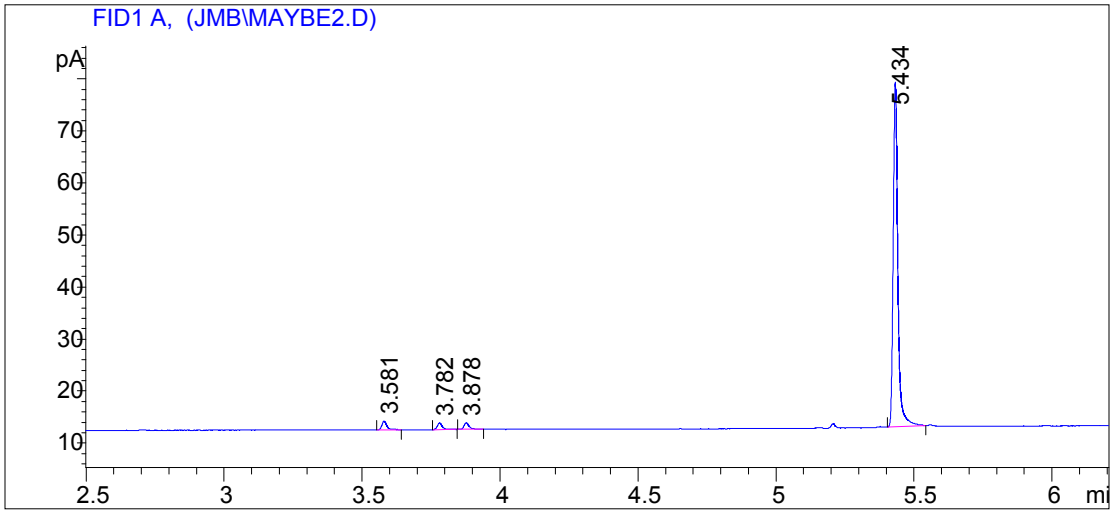


Figure 6: GC chromatogram of 2,4-dichlorophenylnitromethane.

^{1}H NMR ($CDCl_3$) δ 5.55 (s, benzylic 2H), 7.30-7.42 (d, 2, ArH's), 7.52 (s, ArH); IR (KBr) υ_{max}/cm^{-1} 1370, 1554 (two C-NO_2), 2969 (C-H), 3086 (Ar C-H); m.p. 57-58º C

General reaction for the production of phenylnitroethane.

To a 125mL, 3-neck, round bottom flask equipped with a magnetic stirrer, thermometer, condenser, and heating mantle, were charged 75mL of ethylbenzene and 12.6g of zeolite. This mixture was heated to a reaction temperature of 80-85º C with stirring. At reaction temperature, 11mL of 90% nitric acid were added. Reaction was allowed to proceed for at least three hours with continued stirring.

After three hours, the mixture was allowed to cool to room temperature. The reaction mixture was vacuum filtered using a Büchner funnel with #5 Whatman ashless filter circles, and washed with dichloromethane (2 x 10mL).

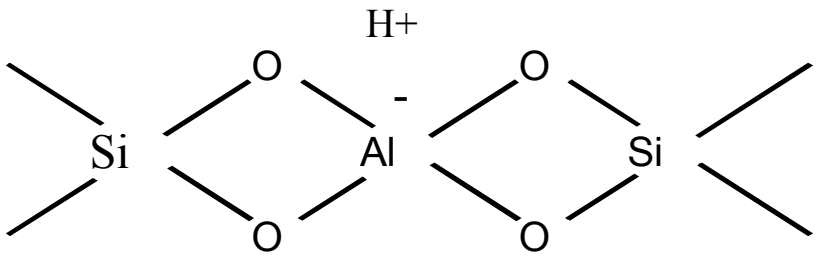
The reaction mixture was extracted using 50% NaOH, aqueous phase was removed and acidified.

After acidification, product extracted from aqueous phase with hexane. Expected product was not present in the organic phase. Base extraction technique appears ineffective at removing the desired product from the crude reaction mixture.

RESULTS AND DISCUSSION

Our investigation of a new and more efficient method for the nitration of toluene began upon reading a report on the use of zeolites during the nitration process. These zeolites, were reported to significantly improve the regioselectivity of the nitration thereby increasing the efficiency. Upon a closer examination, we found what appeared to be a discrepancy dealing with the ability to increase the regioselectivity of the reaction by altering the silica:alumina molar ratio (SAR) of the zeolites. This premise did not seem to follow, as a simple increase in the SAR did not appear to alter the overall physical structure of the zeolites themselves.

To this end, we began by investigating the structure of the zeolites to determine if there was some reason to support the increasing SAR premise. The primary zeolites used during this research are, as stated earlier, molecular sieves that have regular sized channels or pores running throughout the structure. The basic structure is shown below (two dimensionally),



–Chen, N.Y., *et al*. "Molecular transport and reaction in zeolites:design and application of shape selective catalysts". 1994, 32.

As the structure indicates, each aluminum is complexed to a counter ion. When the zeolites are delivered, they can have a variety of counter ions in place, referred to as resident counter ions. The type of counter ion is largely dependent on the manufacturer and the method by which the zeolite was produced. The zeolite used in this research has the resident counter ion tetrapropylammonium ($[N(CH_2CH_2CH_3)_4]^+$). To make effective use of a zeolite during a nitration, it must be activated, which in this case means replacing the resident counter ion with an acidic proton, giving a structure like the one shown in the above diagram. This activation can generally be accomplished by heating the zeolite in air.

The structure also indicates the higher the number of alumina units present within the zeolite, the more active the zeolite would be as there would be a higher population of acidic protons after activation. This seemingly simple observation was the basis of our doubt, as it did not seem to follow that by simply decreasing the overall activity of the zeolite (i.e. increasing the SAR) that the regioselectivity could be improved.

We decided to continue our investigations by replicating the reaction as it was reported by Jayasuriya, et al. in the original U.S. patent study[10]. The goal of the original study had been to minimize the amount of the meta-isomer produced as this isomer was considered an impurity and a contaminant in further synthetic processes. As we attempted to follow the reported parameters and procedures, we found that we could not replicate the reported findings. (See Table 1)

[10] Jayasuriya, K., Damavarapu, R U.S Patent 5 946 638, 1999.

Isomer	U.S. patent study (%)	Conventional Method (%)	Current Zeolite Method (%)
ortho-	17	57	36
meta-	0.19	4	3
para-	83	39	61

Table 1: Comparison of original U.S. patent study, conventional method, and current zeolite method product distribution by GC analysis (area %).

Initially the goal had been to replicate the reported findings and determine the underlying cause of the increase in regioselectivity with increase in SAR. However, we decided instead to determine if the SAR had any effect on the regioselectivity and if it did not what was most responsible for the increase. Since we found that we could not replicate the reported findings, we began to systematically test zeolites with different SAR's as well as different reaction parameters such as temperature, reactant ratios, etc., to determine the effects, if any, these parameters had upon the nitration efficiency.

Before any serious testing could begin, a basic set of reaction parameters needed to be determined as well as a method for analysis. The basic parameters were initially similar to those of the reported reaction as far as temperature and zeolite:toluene ratios were concerned. This course of action was determined in an attempt to minimize the number of parameters being altered at any given point thereby minimizing the chances that the significance of particular change would go unnoticed. To this end, we began by simply using a different zeolite than that used in the reported study to establish a base line from which to work. We chose to use a zeolite with an SAR of 280 (Zeolyst CBV28014) as opposed to that of the zeolite SAR (1000) used in the original study. The 280 was chosen because it represents the "middle of the road" as zeolites are concerned and since it has an SAR significantly higher than the most common forms (30-80) but significantly below that of the study's zeolite (1000). Zeolites with very high SAR's are hard to come by and very expensive. Aluminosilicate zeolites are produced using sand as the basic feedstock, the higher the SAR zeolite desired, the less alumina that can be present. For example, a zeolite with an SAR of 1000 would require 99.83-weight % silica and 0.17-weight % alumina. This indicates that even tiny amounts of alumina can greatly affect

the SAR of a zeolite. This example shows the difficulty in producing zeolites with very high (i.e. 1000) SAR values, as the silica must be extremely pure before the zeolite production begins. The sand used as feedstock must be purified many times to remove these impurities before the zeolite production can begin. The cost of the materials had to be taken into account since this investigation was one attempting to determine a more efficient method.

As stated, the basic parameters, such as temperature and zeolite:toluene ratios were to be maintained. The volume of nitric acid had to be carefully calculated to ensure that polynitration of the aromatic ring did not take place as polynitrated products were not the focus of this study, could have interfered with both analysis and purification and in the extreme, could pose safety risks (i.e. trinitrotoluene). Initial indications of the first few reactions were not promising, as the isomeric distribution was not what had been reported and we noticed that we were producing a byproduct that was interfering with our nitrotoluene (NT) production. (See Fig. 7) The production of the byproduct, phenylnitromethane (PNM), and the meta-isomer presented serious problems, as they could not be easily removed using physical means such as distillation, since their boiling points were relatively close to the desired NT's (ortho- and para-) boiling points. (See Table 2) It was at this point that we decided we needed a better method for determining the amounts of the compounds in question (NT's & PNM) that were being produced during the course of the reaction. We initially used the area percent given by the gas chromatograph to calculate the amounts of products, however this only gives relative amounts. To enable us to convert the to mass, we used decane as an internal standard.

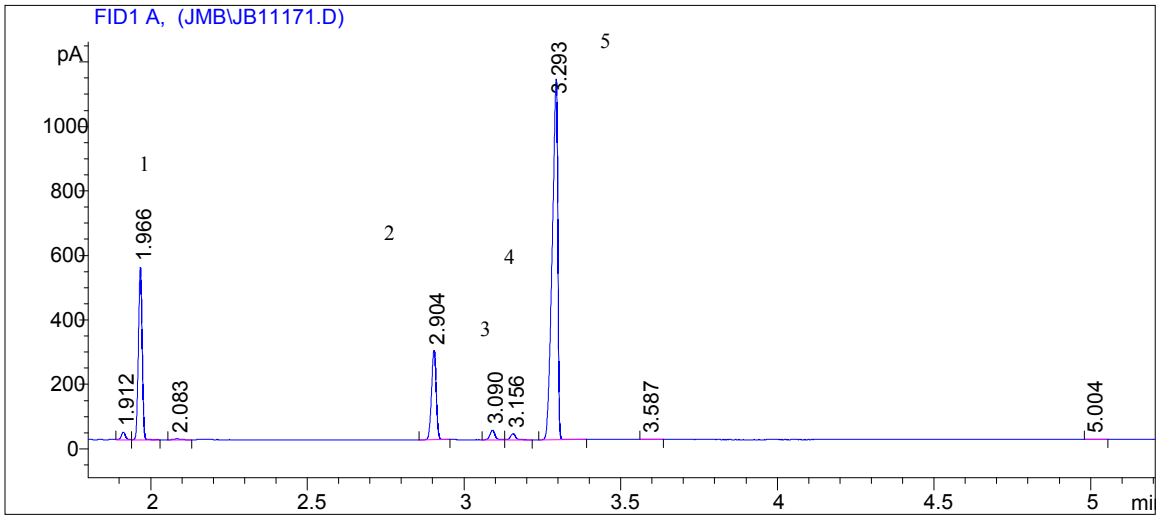


Figure 7: GC chromatogram of a typical zeolite reaction, showing the major products. 1) benzaldehyde, 2) *ortho*-nitrotoluene, 3) phenylnitromethane, 4) *meta*-nitrotoluene, & 5) *para*-nitrotoluene.

Compound	Boiling Points (°C)
ortho-nitrotoluene	225
meta-nitrotoluene	230-231
para-nitrotoluene	238
Phenylnitromethane (PNM)	240

Table 2: Comparison of the individual products of a typical zeolite nitration reaction with their boiling points.

The specific analysis method used can be found under **Experimental**, GC Analysis Method. The use of an internal standard does require the use of a factor that will take into account the differences in response by the detector to a given set of compounds. To this end, a response factor was determined that would allow for a reliable calculation of the amount of product from a given reaction. To take into account the internal standard, response factor and the individual area counts of the NT's, the following equation was derived,

$$(\text{Area NT}/\text{Area Dec})*(\text{mL Dec})*(\text{Fac})= \text{g NT} \qquad (1)$$

where *NT* is the nitrotoluene, *Dec* is the decane, *mL Dec* is milliliters of decane added to the reaction flask, *Fac* is the response factor and *g NT* is the grams of nitrotoluene produced during the reaction. While this form is the one used to calculate the actual number of grams, this equation was used to solve for the response factor by using a known number of grams of nitrotoluene in the sets of standard solutions prepared.

The area counts were determined using the GC and the volume of decane used was a known experimental quantity. The decane is added prior to initiating the reaction and is used as the internal standard since it is unreactive in this process. The volume of decane is used to provide an area count per milliliter relationship. The area counts of both the decane and nitrotoluene are taken from the chromatogram of the particular sample at the same time. A stock solution was prepared by diluting 5g of nitrotoluenes to 25mL using toluene. The nitrotoluenes were set at an o:m:p ratio of 29:2:69, respectively since this is a typical ratio found in the reaction products. The stock was produced using

purchased standards diluted to 25 mL in toluene with the standard ratio given above as percentages.

For example, 69% of the 5g overall total was the *para* isomer and an appropriate amount (3.45g) of the standard was weighed for addition to the stock solution. The same procedure was followed using the *ortho* and *meta* standards. Using varying volumes of the stock solution, two sets of six samples were prepared using two different volumes of decane. The first set of samples were prepared using 50 microliters of decane and stock solution volumes of 0.1, 0.2, 0.4, 1.0, 2.0, and 3.0 mL. Each of the samples was then diluted to 10 mL with toluene. This procedure was repeated for the second set of samples excepting only the volume of decane, which was 200 microliters. All of the samples were then analyzed using a GC. The raw data and calculated values derived can be found in Appendix A. To ensure that the factor held constant over a wide range of decane volumes, a third set of standard solutions was prepared. For the third set of solutions, the mass of the nitrotoluenes were held constant and the volume of decane was varied. The factor was found to be 1.03 and was calculated by taking the overall average values for the factor from the 16 individual solution sets. A single data point, 1.264, was neglected because it was significantly out of range due to experimental error. The data collected indicated that the correction factor would hold constant over a range of decane volumes. This raw data and calculated values can be found in Appendix A. This was a reliable method for comparison of the GC analysis data, but we later found that the decane was being held inside the pores of the zeolite preferential to the nitrotoluenes, causing the effectiveness of the reaction to decrease because the pores were being blocked by the decane. This also skewed some of the initial data concerning the actual yields as the

yield calculations were based on a specified volume of decane and some of that volume was held in the zeolite.

Despite these problems, different reactions could now be performed and easily compared. We repeated the 280 SAR zeolite reaction and achieved similar isomeric distribution. The 1000 SAR gave a little improvement but was similar to the 280 SAR. (See Fig. 8) After these attempts, we decided to alter the temperatures and the zeolite:toluene ratios in an effort to improve yields and isomeric distributions.

The original study indicated that the reaction temperature should be 90-95º C during the nitration. This temperature had not given the desired results, so we decided to vary it, sometimes greatly from the original levels. Our first thought was that the temperature was too high and was pushing the meta-isomer yields higher because of the excess energy. Reactions were undertaken at temperatures below the original study temperatures; at room temperature ≈25º C and at 65-70º C. Neither of these reactions made outstanding improvements to the isomeric distribution or the overall yields of the desired products. (See Fig. 9) The entire set of initial reactions had maintained the zeolite:toluene ratio given by the original study at 1:2 (g/mL). This ratio was reduced in the hopes that more zeolite would be available for the reaction and would improve the isomeric distribution. Reducing the ratio had only negligible effects on the nitrotoluene distribution but did seem to aid in reducing the production of the phenylnitromethane byproduct. (See Fig. 10) Calculated amounts of NT's and PNM add up to more than 100% as each uses the nitric acid and all calculations were based on the volume of nitric acid used.

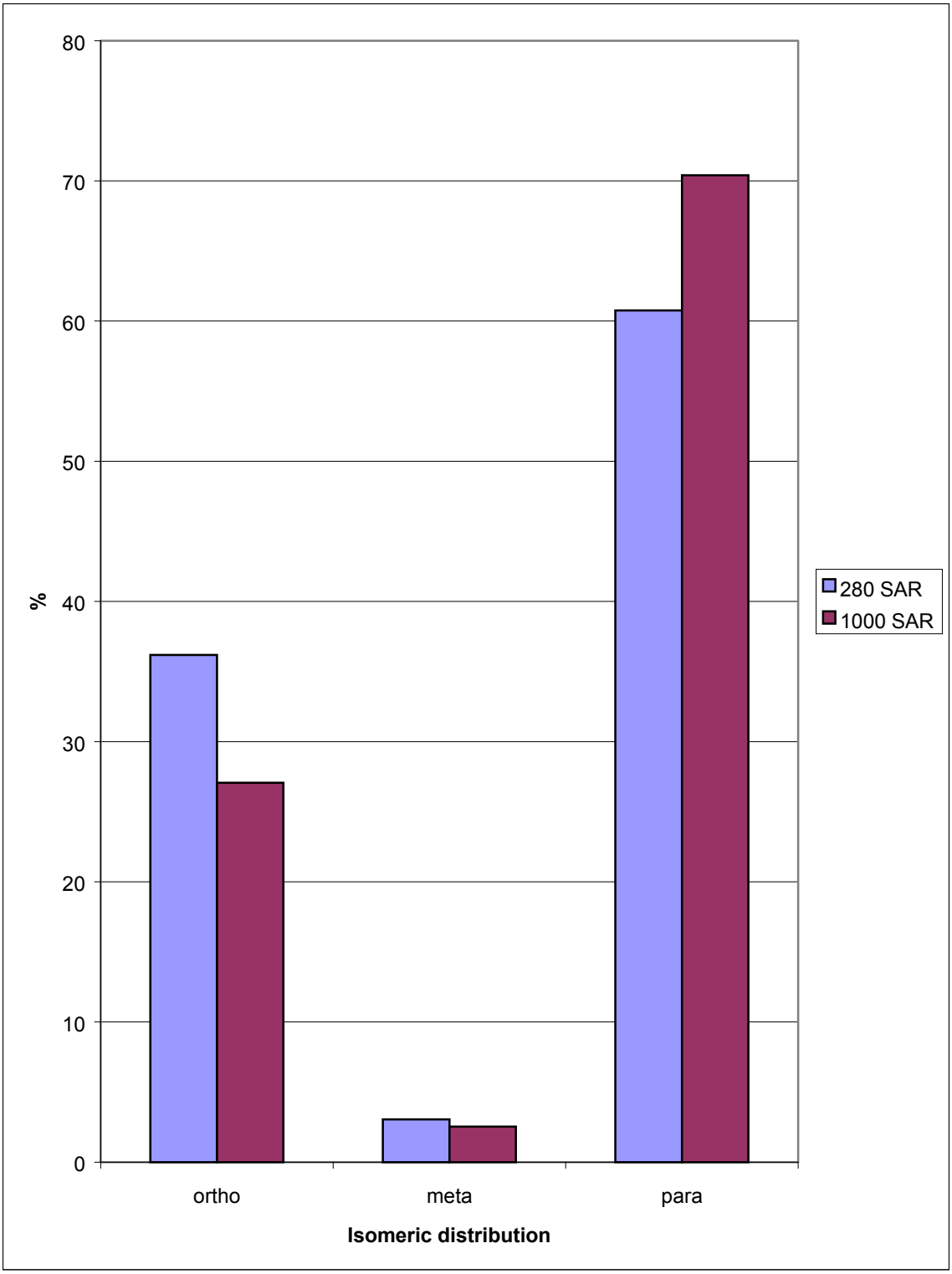


Figure 8: Comparison of isomeric distribution of 280 SAR and 1000 SAR reactions.

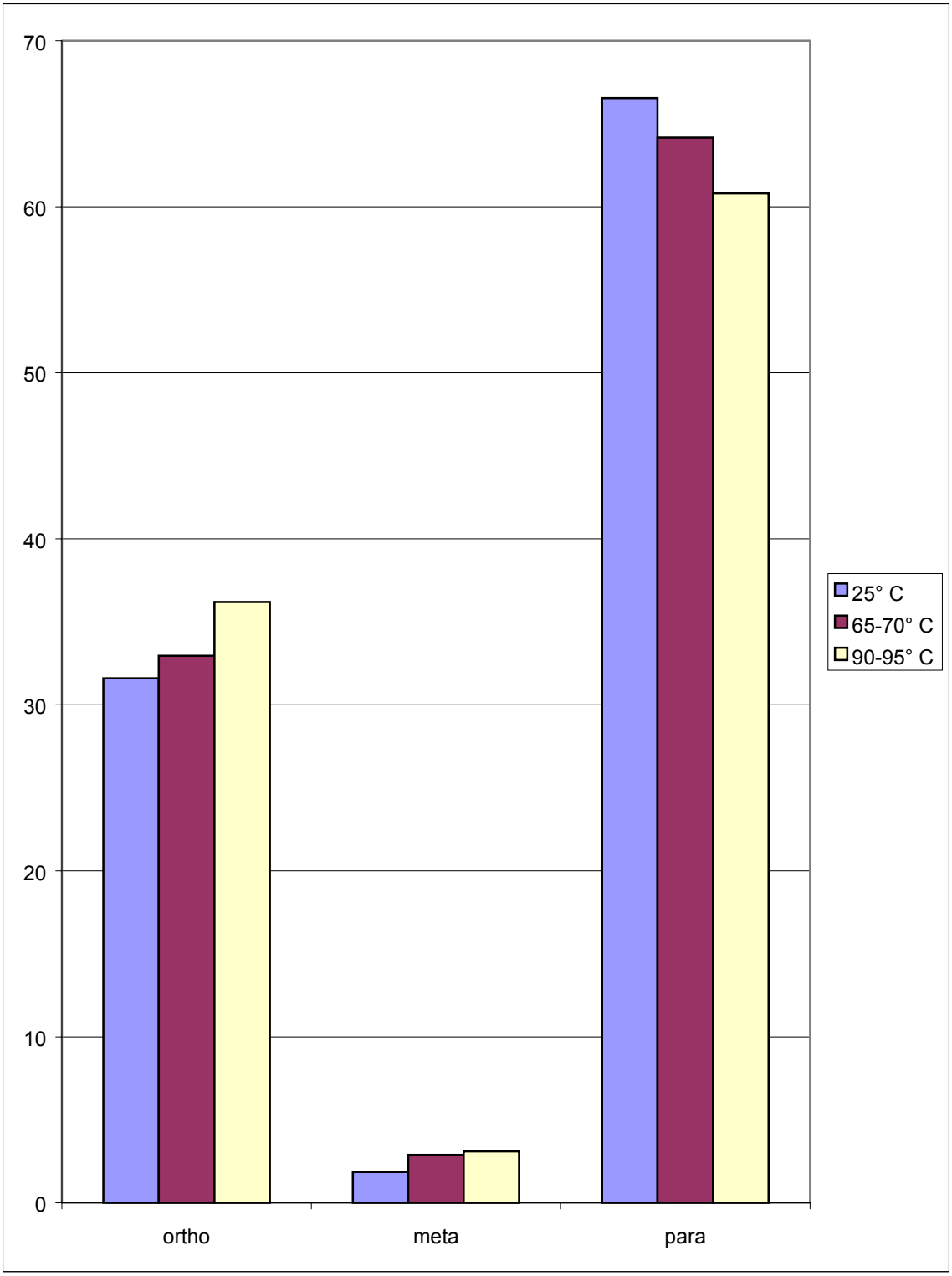


Figure 9: Comparison of isomeric distribution of 280 SAR at 25º C, 65-70º C and 90-95° C.

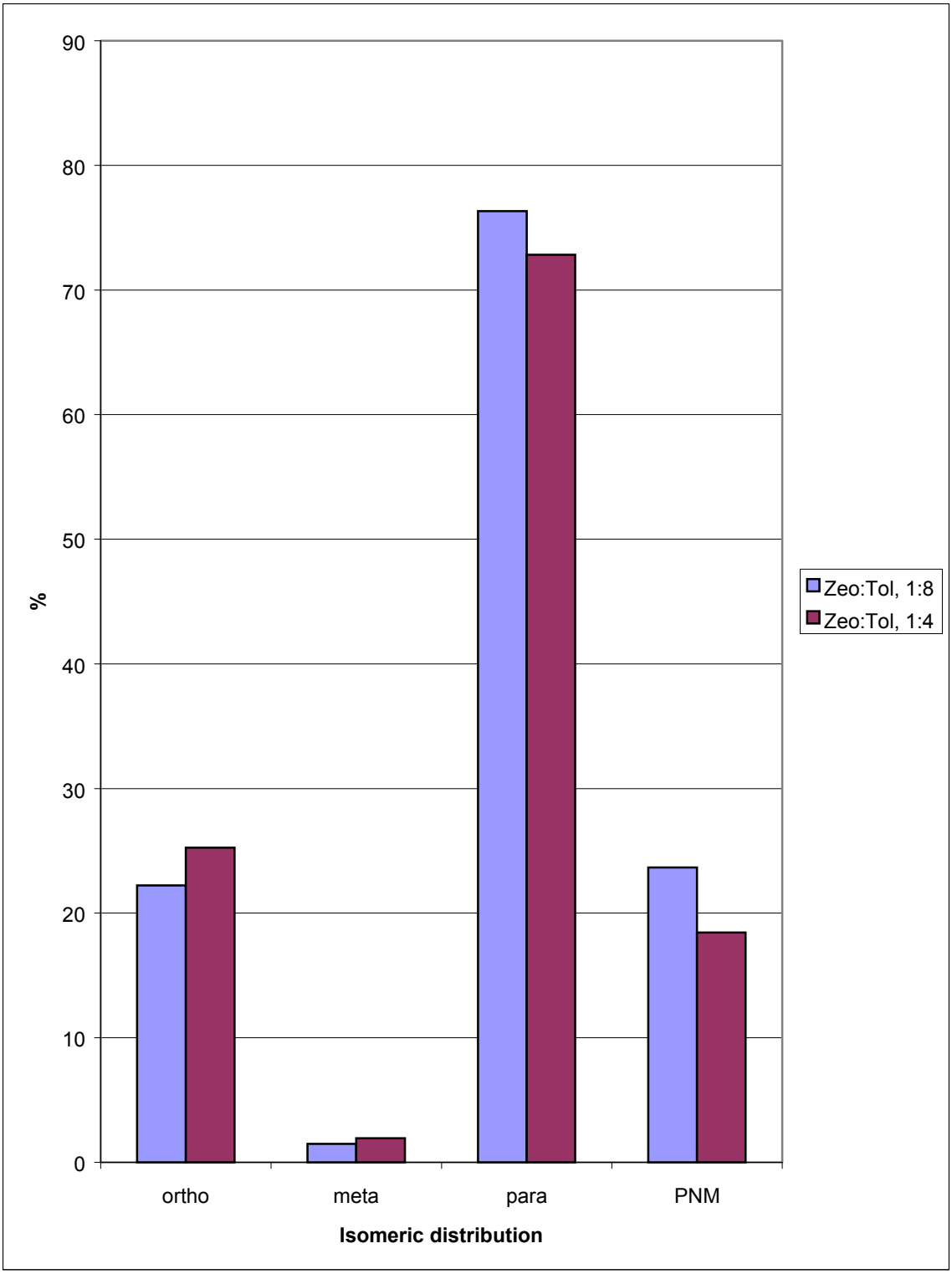


Figure 10: Comparison of isomeric distribution of 280 SAR: Effect of changing the zeolite:toluene ratio.

We ascribe this to decane being trapped by the zeolite, causing all readings to be high.

At this point we decided to go back to the 1000 SAR zeolite with the reduced zeolite:toluene ratios. (See Fig. 11) This proved to be worse that the original trials using the 280 SAR, so we went in the other direction and used an 80 SAR zeolite. Results were much the same as the previous reactions using higher SAR zeolites with respect to the nitrotoluenes. (See Fig. 12) While using a reduced zeolite:toluene ratio we tried to improve the reaction by adding the nitric acid slowly over the course of the reaction. This actually made the nitration less selective than in previous attempts.

Since nothing attempted so far had any overall positive effects using the Zeolyst zeolites, we performed experiments using a different manufacturer's zeolite. Several samples of Tricat zeolites with varying SAR's were tested. The 250-300 SAR normal and low soda forms performed much the same as the Zeolyst samples but the normal soda Tricat 1000 SAR showed significantly different results in that the amount of PNM produced was significantly higher than in previous reactions.

After the relatively poor results of the previous experiments, it was decided that instead of trying to remove both of the undesired byproducts, the meta-isomer and the PNM, we would concentrate on minimizing the production of PNM and then proceed with minimizing the production of the meta-isomer. We found that there was not one but two very different reactions taking place during the nitration. Both of these reactions involved the addition of a nitro group to an existing system but one added the nitro to an

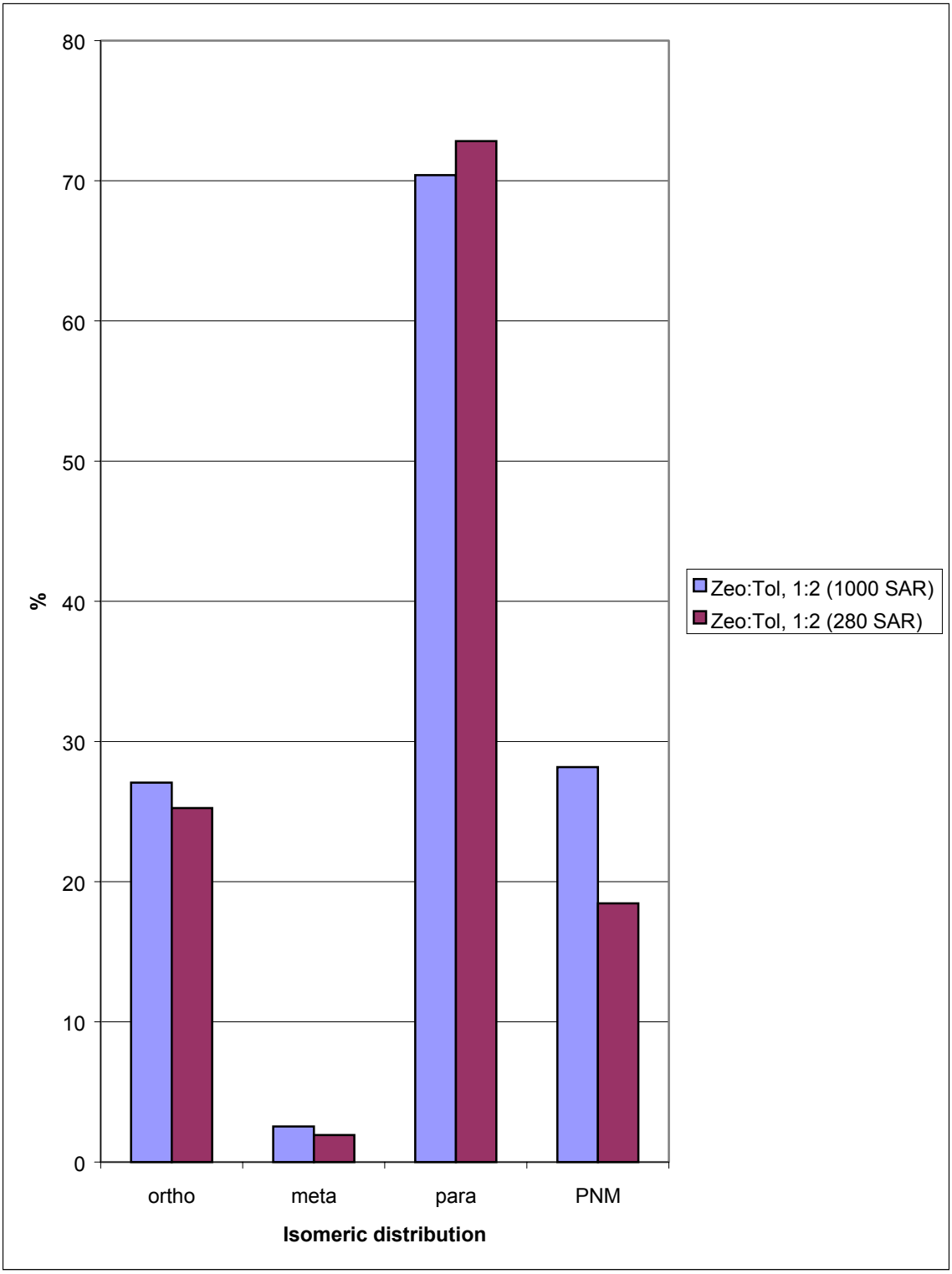


Figure 11: Comparison of the isomeric distribution of 1000 SAR & 280 SAR: Effects of changing the zeolite:toluene ratio.

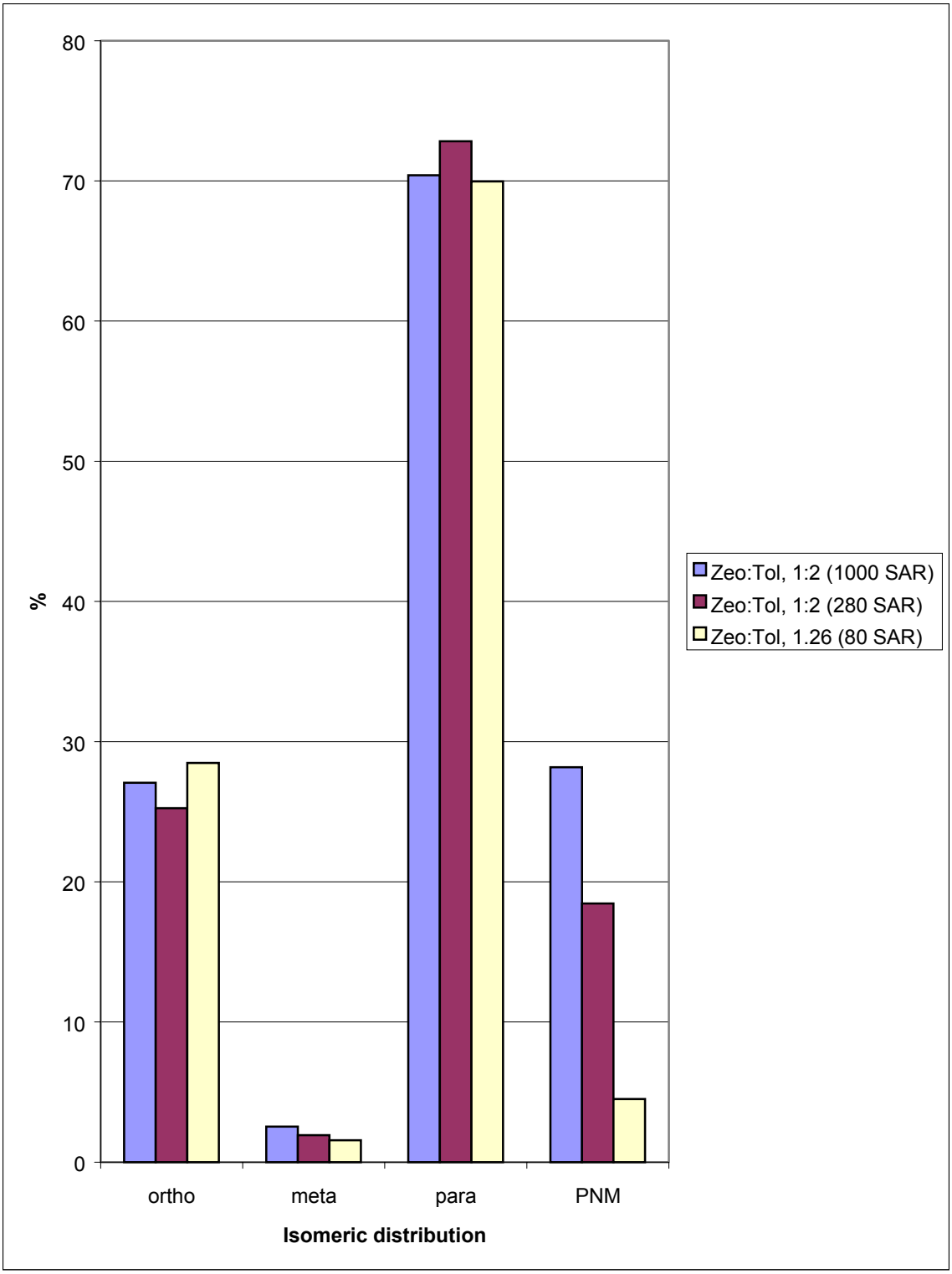


Figure 12: Comparison of the isomeric distribution of 1000 SAR, 280 SAR & 80 SAR: Effects of changing the zeolite:toluene ratio.

aromatic system and one to an aliphatic system. Since the mechanisms for addition to these two systems are very different, it was unclear exactly which mechanism was dominant during our nitration reactions. The nitration of the aromatic system was a straightforward electrophilic aromatic substitution as previously noted, however the nitro addition to the aliphatic system could not be the same type since by its nature an aliphatic system cannot undergo aromatic substitution. Given the materials and the conditions of the reaction, the most plausible type was a radical reaction. Although a radical type reaction would explain much, it was still somewhat of a mystery exactly what was inducing the radical formation and subsequent cascade. It was discovered during a literature review that nitric acid could easily form a nitro radical, nitrogen dioxide as shown below.

$$2\ HNO_3 \Leftrightarrow\ H_2O\ +\ 2\ NO_2\ +\ 1/2\ O_2 \qquad (2)$$

After determining a possible source of the radical, came the more difficult problem of keeping the radical from interfering with the nitration reaction. While trying to find the source of the radical, we noticed that an orange-brown gas that was being evolved during the nitration was always present when the radical product, PNM, was present. The identity of the orange-brown gas was found to be nitrogen dioxide (NO_2). This gas was always evolved immediately after the addition of the nitric acid and it tended to remain in the reaction vessel unless disturbed. If the gas were nitrogen dioxide, remaining in the reaction vessel would give it many opportunities to set up the radical cascade since it was in constant contact over the surface of the toluene. If the amount of

the gas that was maintained over the fluid were reduced then the amount of PNM produced should also be reduced. To this end, a nitrogen sweep was added to the reaction setup in an effort to pull the nitrogen dioxide off without interfering with the overall reaction. Nitrogen was chosen for two reasons; it would be inert in relation to the reaction and it would be less expensive to use nitrogen rather than other inert gases (i.e. helium, argon, etc.). After fitting the reaction with sweep gas, the level of the PNM was reduced. Even though the PNM levels did drop, the amount being produced by the reaction was still up to 4.58%. While the reduction was not complete, directionally it did support the supposition that the gas levels directly affected the amount of PNM and thus supported the theory of a radical reaction concurrent with the electrophilic aromatic substitution. (See Fig. 13)

After adding the nitrogen sweep, we noticed a curious connection between the amount of the meta-isomer and the amount of PNM produced during a given reaction. The general trend appeared to indicate that as PNM levels increased, the meta-isomer levels decreased. (See Fig. 14) There appeared to be some sort of competition between the aromatic substitution and the radical reaction as both of these processes used and depended upon the nitric acid volume. If the competing reactions could be affected, as the nitrogen sweep appeared to indicate, then maybe we could favor the aromatic substitution and reduce the PNM levels even more. It was decided that as much of the gas should be removed as possible and as much of the water that was produced during the course of the reaction. Removing the water might also reduce the amount of meta-isomer being produced as well. Up until now the water content of the reaction had been a secondary consideration, as it would be present if the nitronium ions were present since

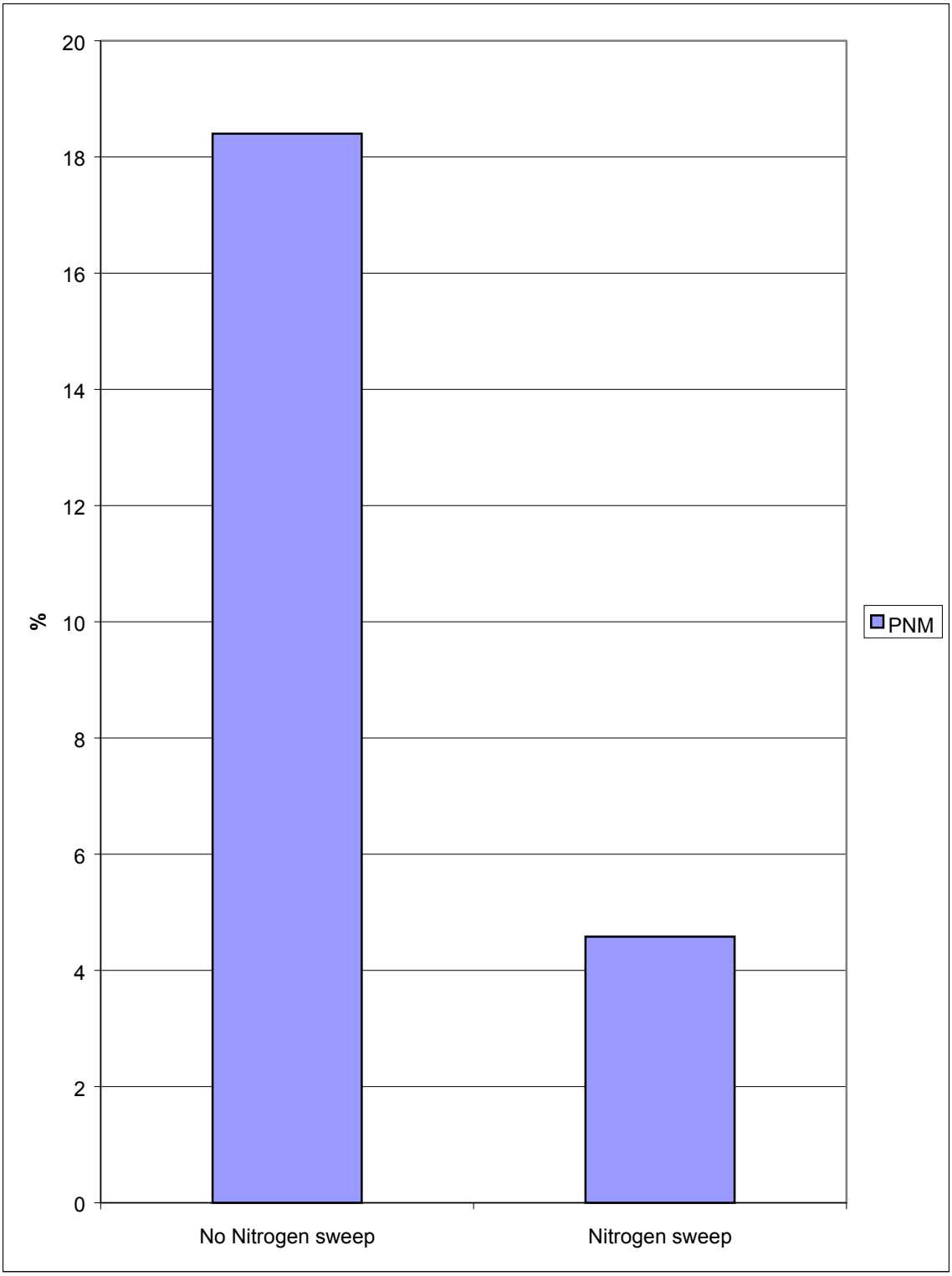


Figure 13: Comparison of PNM production with respect to the use of a nitrogen sweep.

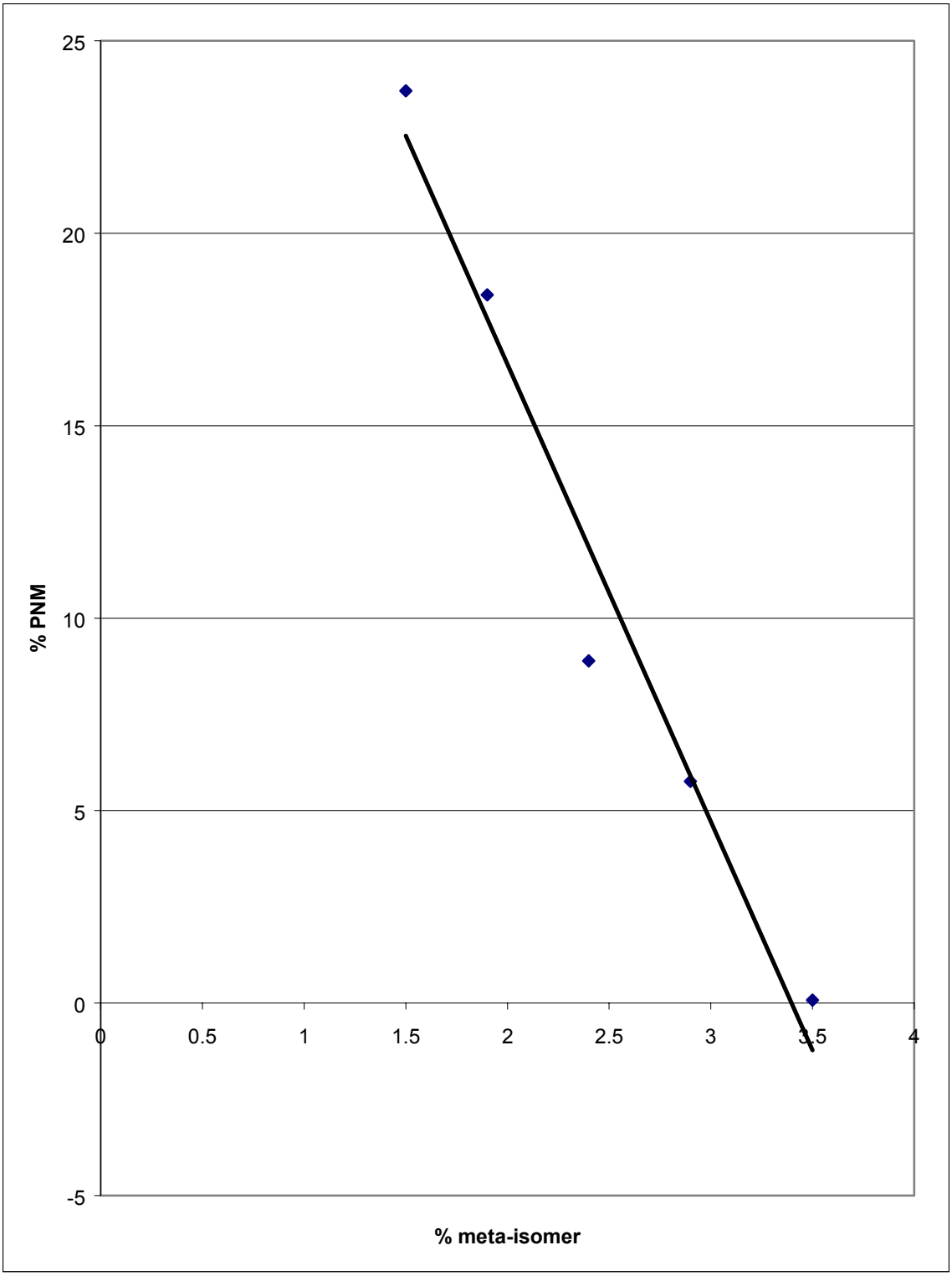


Figure 14: Percent of meta-isomer produced versus percent of PNM produced. (Early conditions; before use of nitrogen sparge)

they were both formed in equimolar quantities. If the water did not have a direct chemical effect on the aromatic substitution, it may have had a simply physical one; if water were to diffuse into the zeolite pores then that would mean fewer pores for the aromatic substitution needs. In order to remove as much of the water as possible, the temperature of the reaction was again increased to approximately 110° C.

The method devised to remove the water and the nitrogen dioxide involved the use of a Dean-Stark (DS) trap and a nitrogen sweep. For the DS trap to be effective in removing the water, the reaction temperature had to be above the boiling point of the toluene/water azeotrope. To remove as much water as possible, it was decided to perform the reaction at reflux temperature with respect to toluene, ≈110º C. Performing the reaction at reflux temperature would help to facilitate the removal of the nitrogen dioxide as well. The use of the reflux did reduce the levels of PNM during the reaction but again the levels were still 1.95%. Since the PNM levels were going down and the meta-isomer levels were not rising as they had in previous attempts, use of the DS trap and reflux temperatures was continued. As the nitrogen sweep had reduced the volume of gas present over the solution, we theorized that removing as much from the solution as possible would improve the reaction even more. Removal of the dissolved nitrogen dioxide required that a nitrogen sparge be used instead of a nitrogen sweep, as the gaseous nitrogen should push the dissolved nitrogen dioxide out of the fluid and the reaction vessel. The addition of the nitrogen sparge did not improve the reaction with respect to the meta-isomer production. The PNM levels were reduced significantly but the meta-isomer levels doubled using the 280 SAR zeolite. (See Fig. 15) Since this could

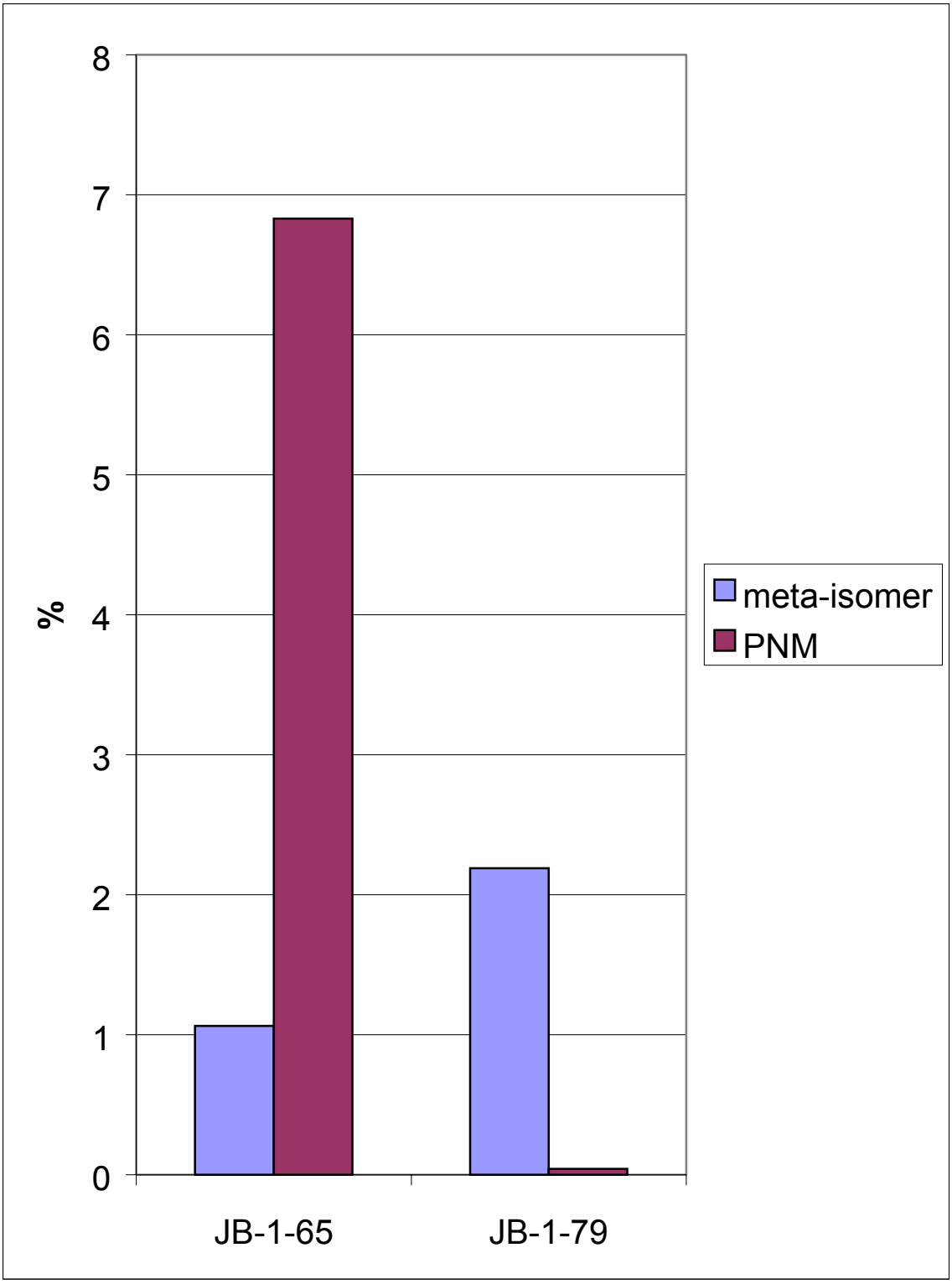


Figure 15: Comparison of meta-isomer production vs. PNM production using 280 SAR using a nitrogen sparge.

have been a result unique to the 280 SAR zeolite, tests were performed on both 80 and 1000 SAR zeolites under the same conditions. The 80 SAR zeolite produced no PNM but maintained the meta-isomer level seen previously, while the 1000 SAR zeolite produced more PNM than the 280 SAR and the 80 SAR, in addition to maintaining the meta-isomer levels seen in both the 280 and 80 SAR zeolites. (See Fig. 16)

Some thought was now given to the possibility that the sulfuric acid played more of a part than simply providing acidic protons during the reaction. To determine the effects, if any beyond protonation, concentrated sulfuric acid was added to the reaction prior to the addition of the nitric acid. (See Fig.17) The results showed that the addition of sulfuric acid to the zeolite assisted reaction increased the amount of the meta-isomer produced, although the level of the PNM was much lower than previously seen using the 280 SAR zeolite. The overall reaction was deemed unsuccessful increase in meta-isomer production and the use of sulfuric was abandoned for use with future zeolite reactions.

The use of reflux-type reactions did not produce better results even though the water was being removed. However, the use of the nitrogen sparge did seem to be promising so a series of tests were performed using the nitrogen sparge but at the temperature given by the original study of 90-95º C. The tests were conducted using the three Zeolyst zeolites (80, 280, and 1000 SAR) under the same conditions each time. This was done because the data suggests that none of the three zeolites tested gives an inherently better isomeric distribution, but the data did tell a very different story as far as the PNM was concerned, specifically the lower the SAR the less PNM is produced. As we still had not made a definite connection between the SAR and the PNM production

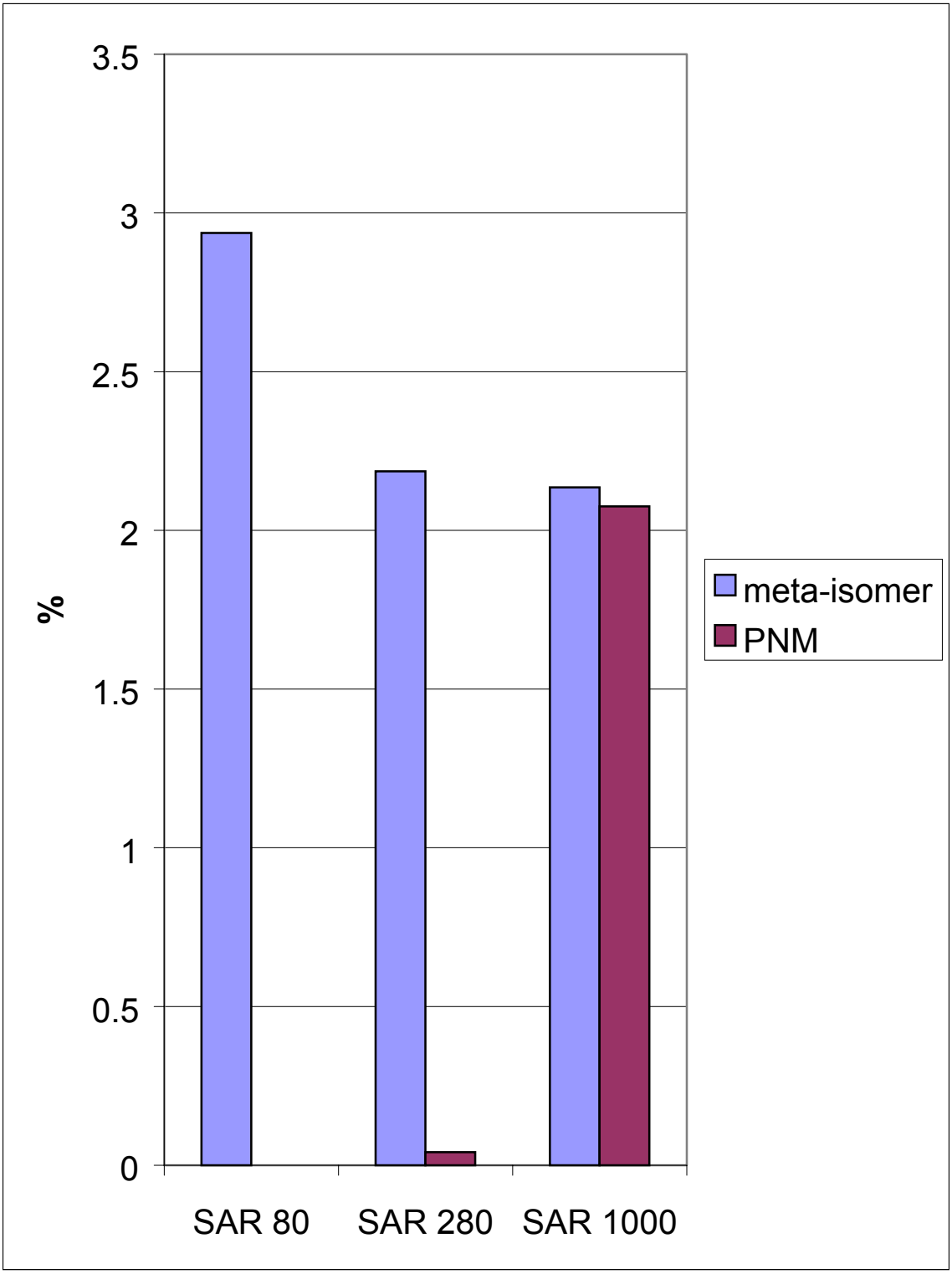


Figure 16: Comparison of meta-isomer production vs. PNM production using 80 SAR, 280 SAR, 1000 SAR.

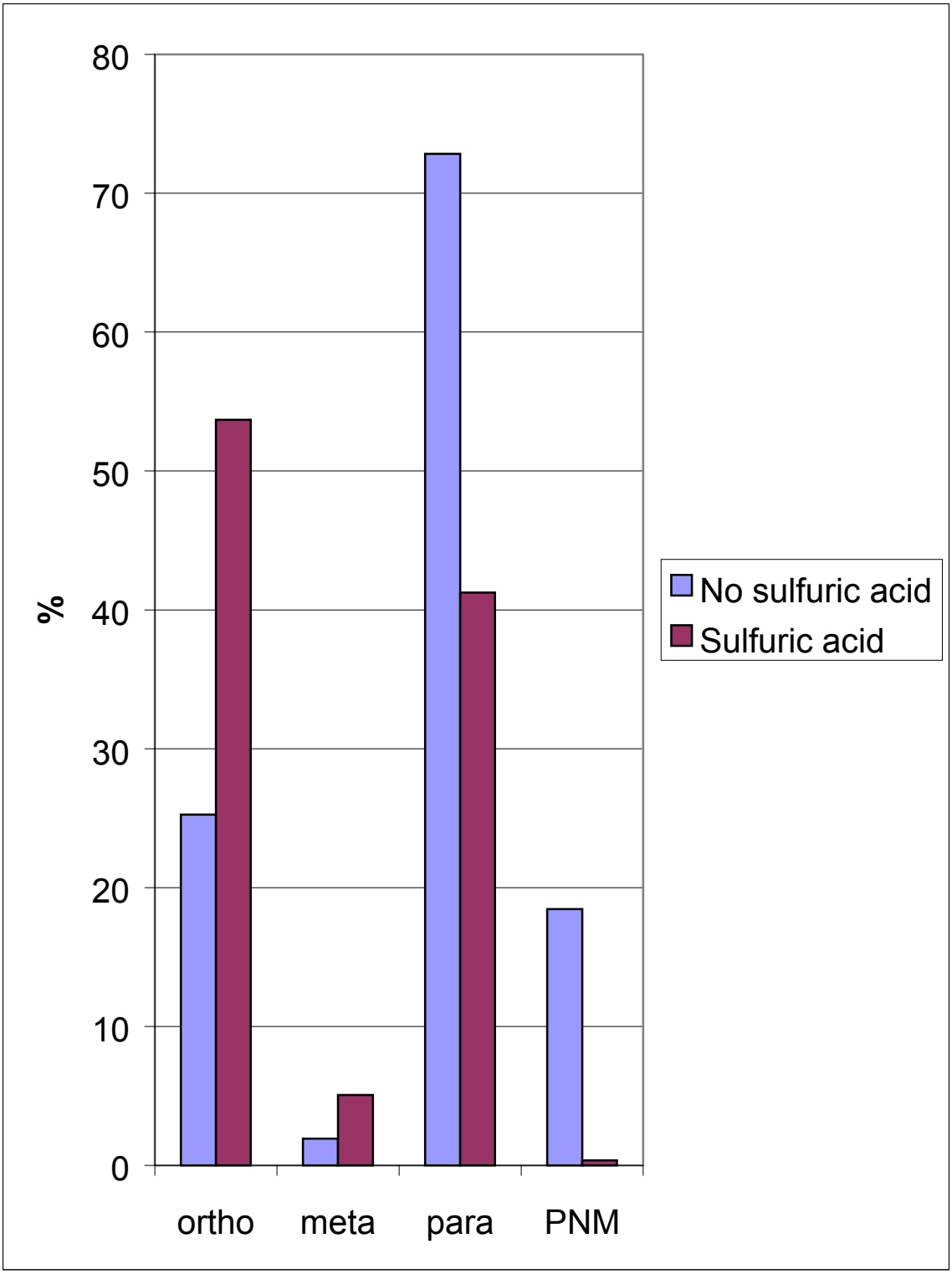


Figure 17: Comparison of the isomeric distribution and PNM production after addition of sulfuric acid to zeolite reaction.

we questioned whether the temperature at which we were calcining the zeolites was not sufficient to remove the resident counter ion. This follows given that the resident counter ions could create a "log jam" that would keep the toluene molecules inside the zeolite or keep them from getting into the pores themselves. If this were true then the counter ions could be impeding the aromatic nitration and giving the remaining radicals a chance to react with the toluene. To eliminate this possibility, the zeolites were now calcined overnight at 550º C in a muffle furnace. (See Fig. 18) This temperature, it was felt, would be sufficient to remove the resident counter ion but would not adversely affect the zeolite. The reactions illustrated in Fig. 18 were not directly comparable since other parameters were changed in addition the calcine temperature and although no discernible trend of improvement was noted, the zeolites were calcinated at 550° C for the remainder of this research project. While the addition of the nitrogen sparge had been effective at reducing the amount of PNM produced, the levels were still unacceptably high given that this compound could not be easily removed and would be a contaminant in any further reaction. We still thought that the removal of the radicals in the reaction mixture would reduce the level of PNM if not eliminate it all together.

Instead of trying to completely force the radicals (i.e. nitrogen dioxide) out of the solution, we thought of adding a radical scavenger to remove as many of the radicals as possible in addition to the removal by sparging. The scavenger used was 2,6-di-*t*-butyl-4-hydroxy toluene (BHT), but the use of the BHT radical scavenger did not reduce the PNM produced, and did in fact show an increase in the amount of PNM over the same reaction without the radical scavenger. (See Fig. 19)

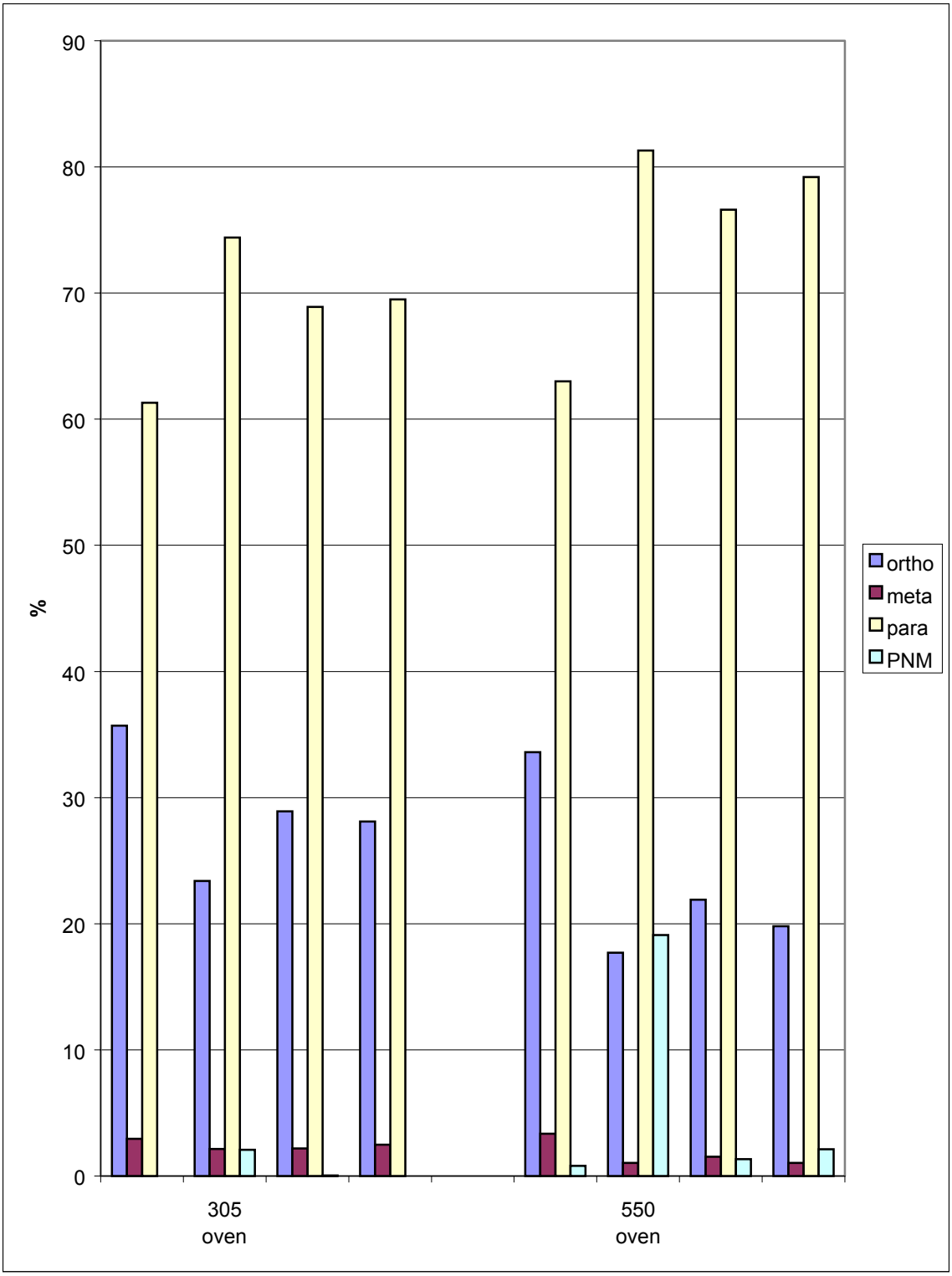


Figure 18: Comparison of product distribution using 305° C and 550° C temperatures for calcinating zeolites.

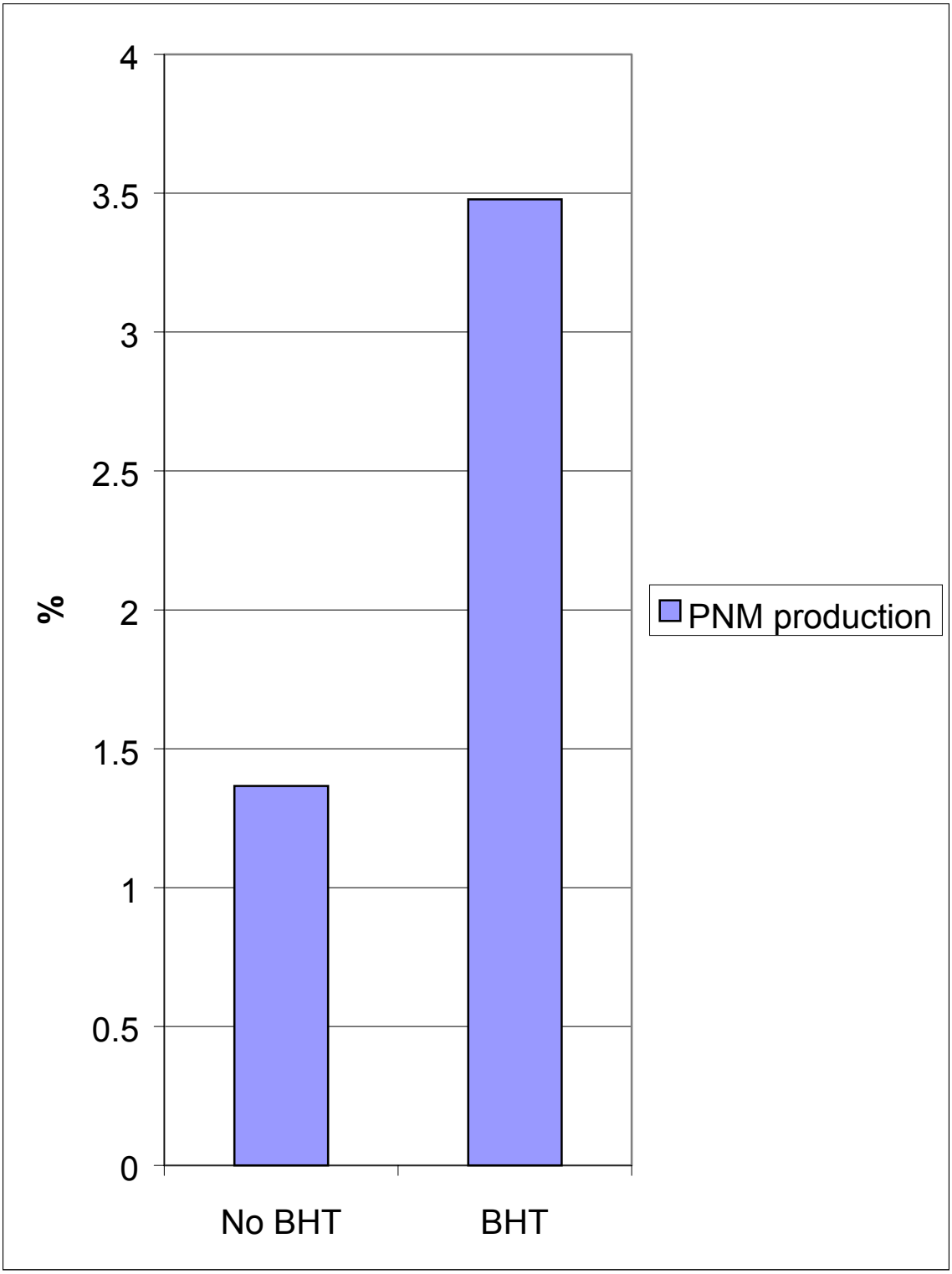


Figure 19: PNM production based on the addition of radical scavenger BHT.

At higher temperatures even more PNM was produced. (See Fig. 20) This particular scavenger was used because of both its scavenging abilities, its size, too large for the zeolite pores, and its relative unreactivity under these conditions. Since the BHT did not reduce the amount of PNM produced and it actually increased the production compared to the same reaction without the BHT, the use of a radical scavenger was abandoned for future reactions. Peng, et al, reported the use of a radical scavenger, *m*-dinitrobenzene, while investigating the use zeolite assisted nitration of neat toluene and chlorobenzene with a nitrogen dioxide/molecular oxygen system. The use of the radical scavenger offered no apparent improvement in the isomeric distribution.[41]

Another compound was added to the reaction in an attempt to reduce the reactivity of the surface of the zeolites. During the course of a zeolite reaction, the surface of the zeolites might also have active sites that are not under any size exclusion restraints imparted by the pore size. The surface activity can have a direct effect on the production of both nitrotoluenes and PNM. To reduce the activity of the surface sites, tetraethoxysilane (TEOS) was used. The TEOS would react with the surface hydroxyls and by this reaction render these sites unreactive to the nitration reaction; the TEOS would in effect coat the surface with unreactive material thereby reducing the production of the surface sites. The addition of the TEOS showed negligible improvement over previous reactions and was therefore abandoned.

A trend had been identified that connected the amount of PNM produced to the SAR value of the zeolite in use. In general it appeared that the higher the SAR the more PNM produced. This trend was not linear under the given reaction conditions but we

[41] Peng, X., Suzuki, H., Lu, C. *Tetrahedron Letters*. **42**, 4357-4359 (2001).

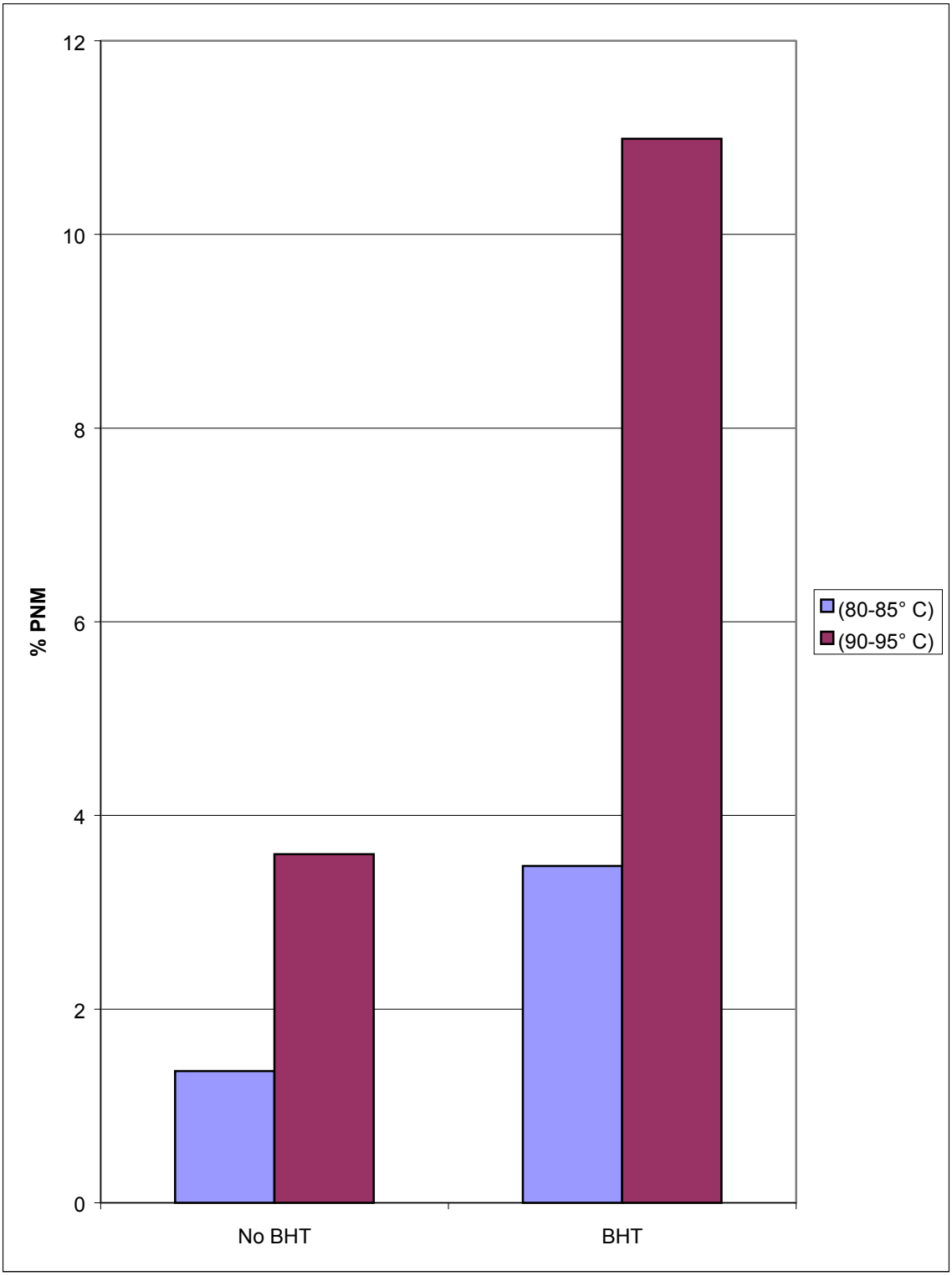


Figure 20: Comparison of PNM production using a radical scavenger (BHT) with respect to temperature.

thought that it was an important trend nonetheless. To determine if the trend, held, it was decided to test a zeolite with a lower SAR than had been tested previously. The Zeolyst 30 SAR zeolite was tested under the reaction conditions that had provided the most positive results using the other zeolites. At this time we learned that the trend we had observed basically fell apart as the SAR 30 zeolite produced more PNM than the SAR 80 zeolite while giving approximately the same isomeric distribution and amount of meta-isomer produced. (See Fig. 21)

To this point, the best overall reactions that had been performed had been those using the Zeolyst 280 SAR zeolite therefore this particular zeolite became the focus of our efforts at improving the reaction. With this in mind, a repetition of an earlier reaction using a slow add or top charge of the nitric acid over the course of the reaction was undertaken using the improved conditions and the SAR 280 zeolite again. While the results were better than the first attempt without sparging, isomeric distribution was worse. The amount of PNM produced was slightly less but the top charge method was discarded due to the poorer isomeric distribution.

This left the nitric acid a possible cause of the PNM. The nitric acid was the source of the nitrogen dioxide and therefore the bulk of the radicals formed during the reaction. After a literature search of the uses of nitric acid, a method was found that could help reduce the amount of radicals formed by the nitric acid without substantially changing the nitric acid itself. It was reported that the nitric acid being used for the nitration reactions was contaminated before it was even used by the nitrogen dioxide. The reason for this was very simple; the nitric acid used was at a concentration (>90%) that started to produce the nitrogen dioxide while it was still in the bottle.

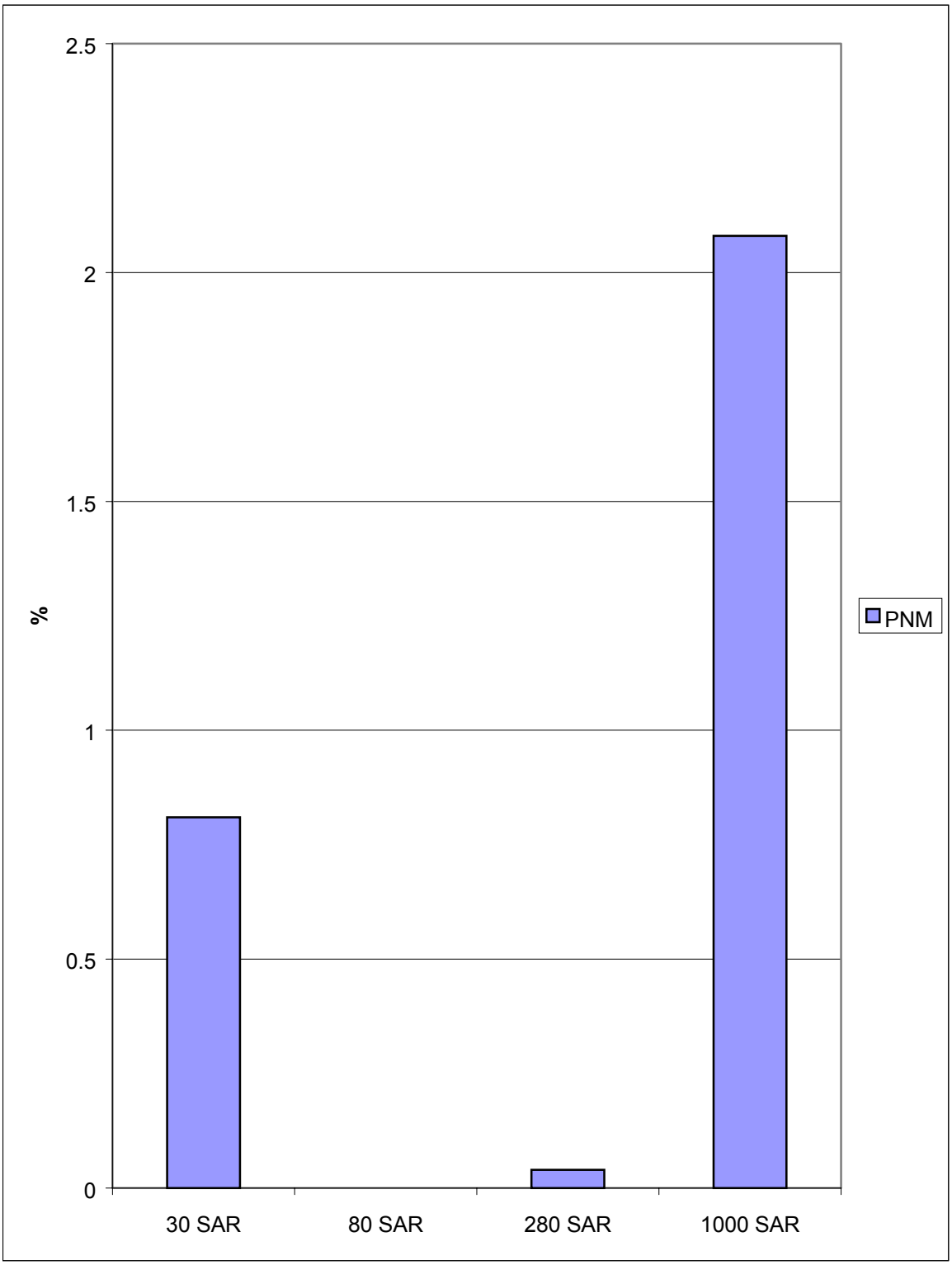


Figure 21: PNM production with respect to SAR (30, 80, 280 & 1000).

If the nitrogen dioxide was already being formed in the nitric acid before it was added, then the reaction was already at a disadvantage in the competition between the aromatic substitution and the radical cascade. To combat the initial presence of the nitrogen dioxide, a method for "cleaning" the nitric acid was found[40]; to 21.5mL of 90% nitric acid was added 0.1g of urea and the whole solution was air sparged for thirty minutes. After this procedure the color of the nitric acid changed from pale yellow to clear. After preparing the nitric acid by the above method, a reaction was performed to determine the effectiveness of the now purified nitric acid. The reaction conditions used were those of the original study and the data suggested that the purification of the nitric acid would not be enough by itself to reduce the levels of PNM produced. (See Fig. 22) Even though the purified nitric acid did not cure the PNM problems, it did represent a positive step and if it could be coupled with the best of the reaction conditions determined then the possibility of a low PNM reaction was good. Once the PNM problem was under control then the meta-isomer problem could be approached.

To determine if the use of the purified nitric acid was effective, a reaction was performed using the purified nitric acid with the updated reaction conditions (i.e. nitrogen sparge, zeolite:toluene ratio), excepting only the temperature, which was kept at 90-95º C. The results indicated that the use of the purified nitric acid was a positive addition to the reaction conditions as the levels of PNM were significantly reduced compared to the previous attempt. After seeing the results of using a temperature range we thought was too high, we repeated the reaction using a slightly cooler temperature, 80-85º C, and the results were even better than at the original temperature. (See Fig. 23)

[40] Freeman, P., Shepard, I.G. *Org. Syn.,* **43**, 84 (1963).

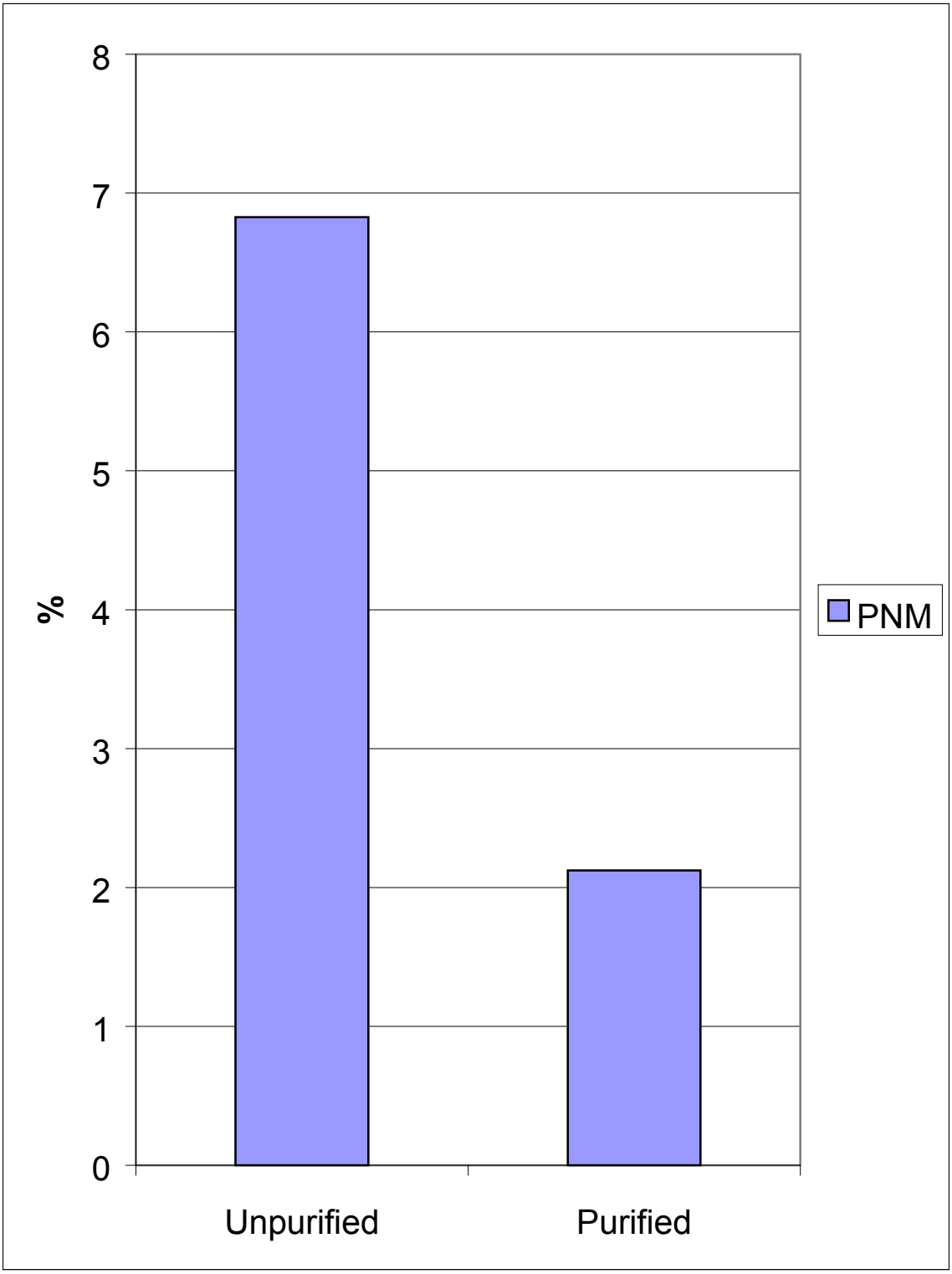


Figure 22: PNM production as related to the purification of the nitric acid by addition of urea with air sparging at a reaction temperature of 90-95° C.

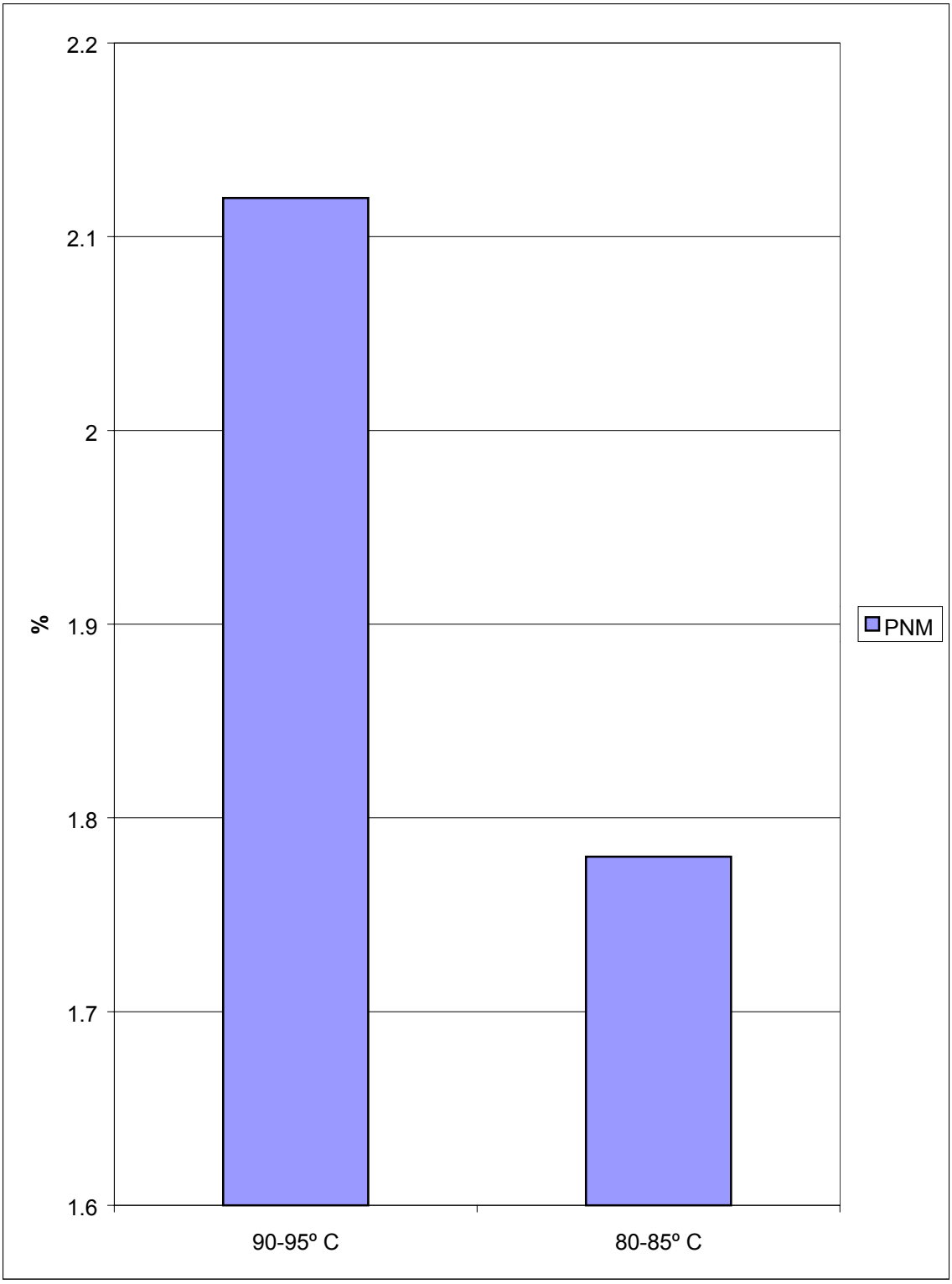


Figure 23: PNM production as related to temperature using purified nitric acid.

It was at this time that we decided to use the cooler temperature of 80-85º C since we saw no advantage with using higher temperatures.

Now that the nitric acid had been purified to remove the nitrogen dioxide, the next step was to determine if the zeolites also had some responsibility for the production of PNM and to determine if a zeolite from a different manufacturer could improve the isomeric distribution. For this determination a series of zeolites from different manufacturers were tested under the same reaction conditions and using the same reaction parameters (i.e. toluene volume, purified nitric acid, etc.). These different zeolites gave a broad range of PNM produced, meta-isomer production and isomeric distribution but none of them improved the overall reaction so these reactions were used only for reference and were not repeated because the Zeolyst zeolites gave comparable or better results.

After completing the testing of the different zeolites, the reaction that had produced the best results was repeated to determine if these results had been a fluke or were reproducible. The results were in fact reproducible (See Fig. 24) and showed the overall best isomeric distribution, the least amount of meta-isomer and a relatively low amount of PNM. To give a reference point for the best reaction, it was decided to perform the same reaction, except that no zeolite would be used. The non-zeolite reaction gave expectedly bad figures for the isomeric distribution and for the amount of the meta-isomer produced but surprisingly, the PNM levels were very low, which led us to believe that the zeolite itself played a part in the production of the PNM. (See Fig. 25)

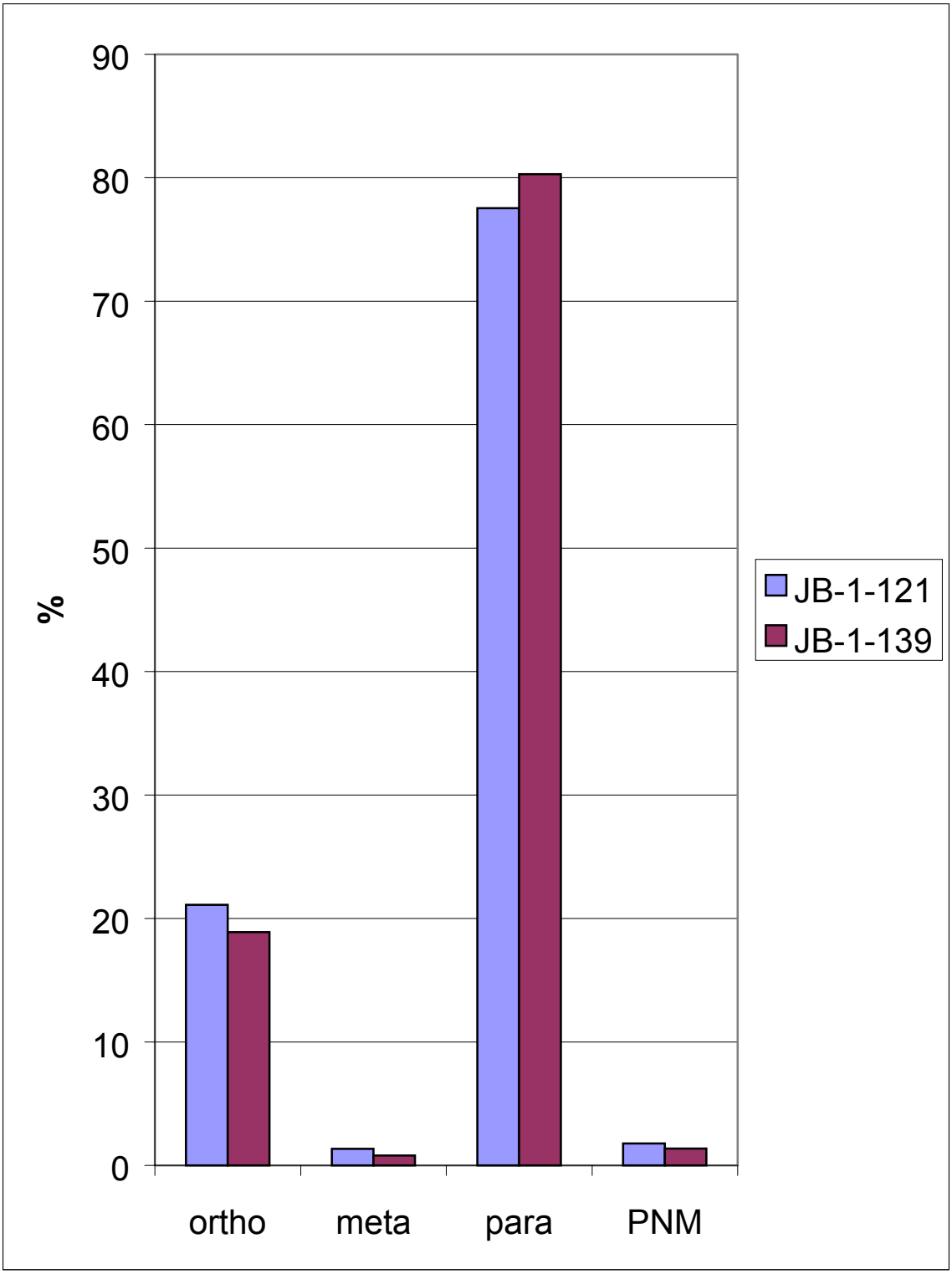


Figure 24: Comparison of the reproducibility of the best overall nitration reactions with respect to the isomeric distribution.

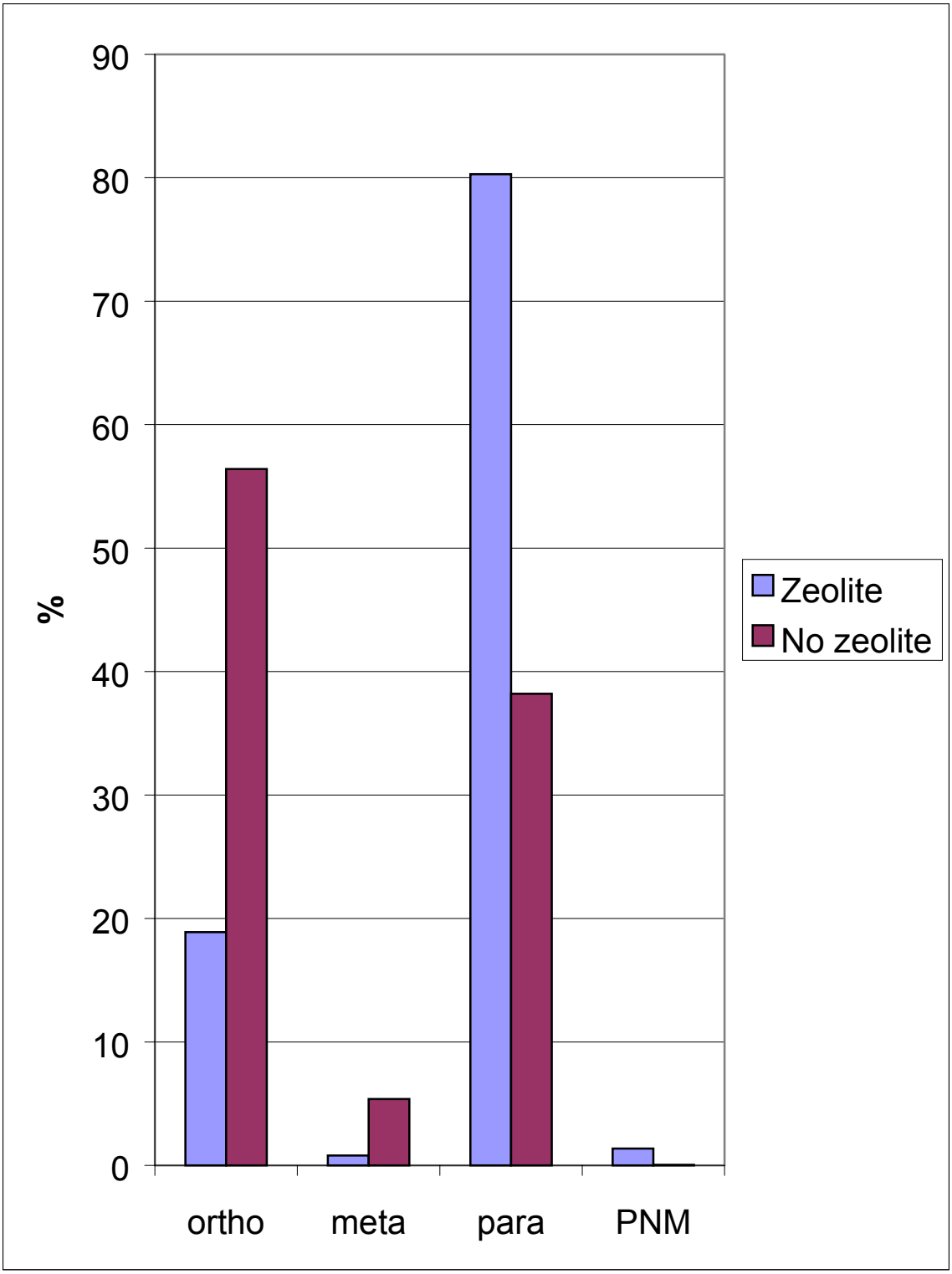


Figure 25: Isomeric distribution and PNM production with respect to the presence of zeolite.

In order to determine the role of the zeolite, we needed to know exactly what was in the structure besides the silica and alumina. After consulting with the manufacturer, we found that the zeolites might contain varying amounts of trace iron impurities as well as the silica and alumina. This would fit the data already collected since the reaction that had no zeolite produced very little PNM while the zeolite reactions produced varying amounts of PNM depending on the zeolite. To determine if the iron were catalyzing the formation of radicals and adding to the radical cascade, a study of the amount of iron contained in the zeolites was undertaken. The study involved digesting the Zeolyst zeolites (80, 280, and 1000 SAR's) in a mixture of hydrochloric and hydrofluoric acids.

After digestion the solutions were analyzed using a flame atomic absorbance spectrometer. The results of the testing indicated that there was iron present in the zeolite but it was present in only low (<10) part per million (ppm) levels.

We did not see a trend between the iron levels and the production of PNM during the reaction. It is also a possibility that another metal may be responsible for the radical catalysis. It is also distinct possibility that the radical catalysis is not due to trace metals at all but is a property of the zeolites themselves.

After testing to determine the effects, if any, of iron contained in the zeolite structure, we reached an impasse as to how to improve the reaction any further. Up to this point the reactions using zeolites were far superior to the non-zeolite reactions but had not lived up to the expectations. We thought that it might be possible to increase not only the selectivity but also reduce the production of the PNM. So far it had been discerned that the selectivity was mostly a function of the pore size and the ability of the reactants to diffuse into those pores to undergo the aromatic substitution. If the aromatic

substitutions were taking place outside of the pores in the general toluene solution then the ortho- and meta-isomers could be easily formed. This is the central point of this entire project, as the nitration is most selective when it takes place inside the zeolite pores. Outside of the zeolite pores the radical cascade would be likely since the zeolites preferentially formed the nitronium ions not the nitrogen dioxide. If the nitric acid, and hence the nitronium ions, could be placed into the zeolite structure before the toluene was added then the aromatic substitution might be much more preferential, thereby reducing the undesired byproducts and isomers.

To this end, a method for "pre-treating" the zeolite with nitric acid was developed. This method involved using a non-reactive carrier medium to bring the nitric acid into the zeolites and then adding the toluene to begin the aromatic substitutions. The chosen carrier was chloroform as it was inert with respect to the nitration reaction and it could be easily removed for purification under reduced pressure distillation.

Testing of this method indicated that the levels of both PNM and the meta-isomer were significantly reduced. (See Fig. 26) The meta-isomer levels were seen to be at their lowest since testing began, and the reduction is attributed to reduced amount of nitronium ions outside the zeolite pores and as there were fewer nitronium ions outside the zeolites there was less chance of adding to the meta position. The isomeric distribution was also significantly improved as more than 80% of the NT's were of the para-isomer. The PNM levels were significantly lower and this was most likely due to the fact that the nitrogen dioxide seemed to be evolved before the toluene was added and therefore did not have the chance to react with toluene as it had previously. This reaction proved to be the best

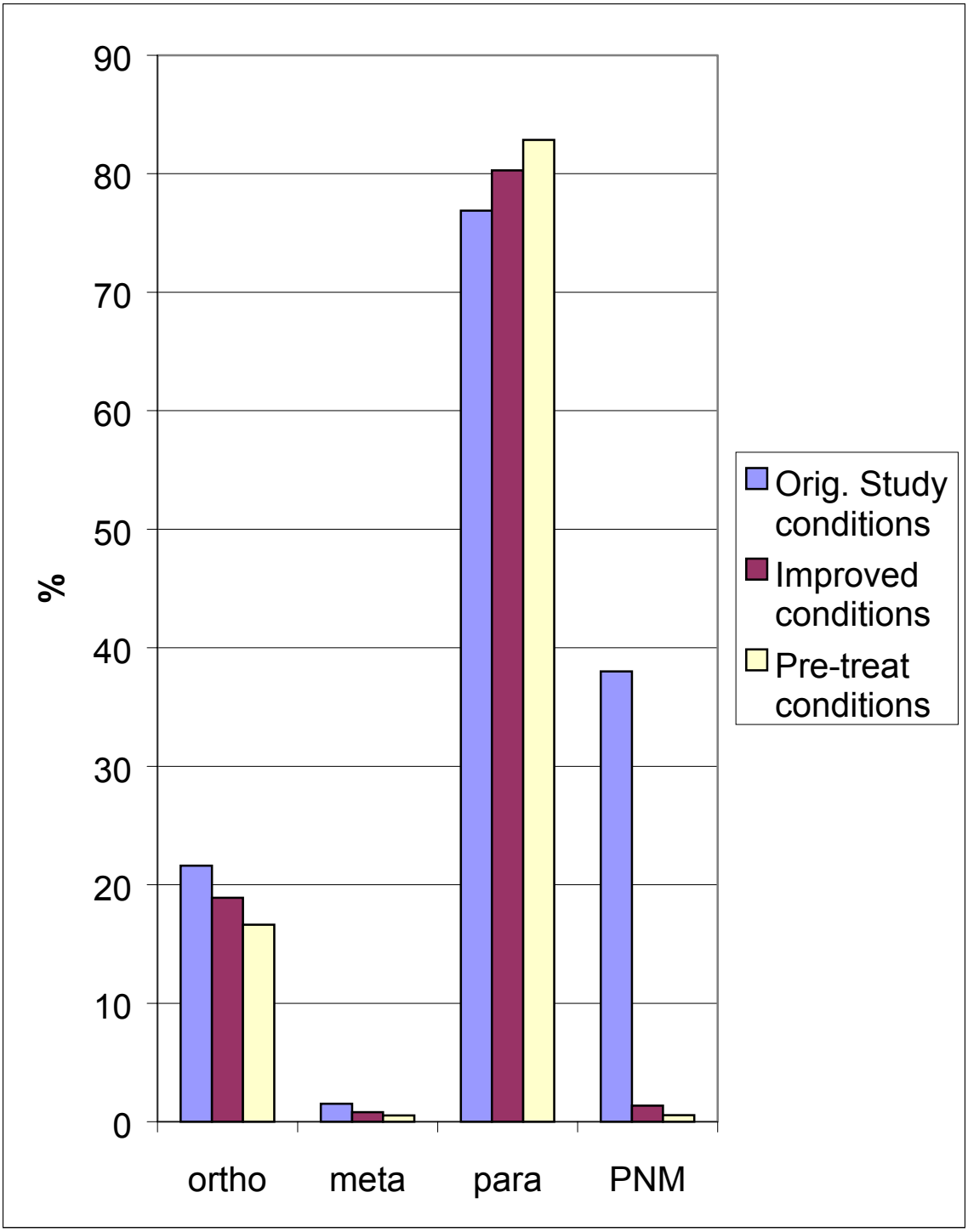


Figure 26: Comparison of the isomeric distribution and PNM production with respect to improved reaction conditions (temperature, sparging, nitric acid purification, and pre-treatment).

one tested so far and was repeated to ensure that the results were not aberrant; the results confirmed that this reaction was the optimal method for the production of nitrotoluenes.

The optimization of the zeolite assisted aromatic nitration of toluene was found to involve more than simply using a higher SAR zeolite. Using a higher SAR did not reduce the production of the meta-isomer or the PNM and in fact, the higher SAR zeolites tended to produce more of the undesired meta-isomer and PNM. The optimized nitration involved the use of a lower temperature than previously reported, a nitrogen sparge to remove nitrogen dioxide from the reaction mixture, and pretreatment of zeolite with purified nitric acid. These conditions contributed to an isomeric distribution of 16.6% *ortho*-, 0.52% *meta*-, and 82.8% *para*-, with a PNM level of 0.55%.

During the previous discussion, we referred to the peak #3 impurity as phenylnitromethane (PNM). This assignment was initially tentative and based on crude mass spectrometry data. This data was gathered while attempting to determine what the impurities were in the first set of reactions undertaken. In order to determine the identity of the impurity we needed to compare it to an authentic sample. In the course of the attempts to improve the nitration reaction there was always an attempt to reduce or eliminate the PNM that was produced; upon further investigation of this compound it was found that the PNM was not a commonly produced chemical and could not be purchased commercially. After all of the attempts to eliminate the PNM, we now set our sights on not only making the PNM but to optimize a reaction to produce it. With the data that had been collected regarding the nitration reaction, it seemed only a small step to shift the reaction over to produce the PNM instead of the nitrotoluenes.

The first task would be to produce PNM for use as a standard for analysis purposes. We were aware of an *Organic Synthesis*[42] preparation but this required a complicated and lengthy synthesis that involved the use of chemicals, which were not only expensive but also difficult and sometimes dangerous to handle. We attempted to synthesize an authentic sample using the method reported by Baruah, et al.[38] The reaction was performed a number of times and none of them produced an isolable amount of PNM for use as a standard. The first attempts followed the reported method and when these met with failure the subsequent tests involved altering the conditions and parameters. Table 3 gives a complete description of the parameters and conditions used.

None of the attempts proved useful in that they mostly produced benzaldehyde and only trace amounts of PNM. The last attempt was radically different and resembles the Kornblum reaction, which will be discussed later. The similarity of the two reactions indicates the sensitivity of the Kornblum reaction, as the JB-2-17c reaction produced no PNM while the Kornblum produced a relatively large amount. At this point, we contacted the authors of the report in an effort to determine why the reaction was not performing as reported. The authors of the Baruah method let us know that they could not reproduce the results and directed us to work by Makosza.

[42] Babers, F., Black, A. *Org. Syn.* CV 2, 512.

Reaction Reference	Volume Benzyl Alcohol (mL)	Volume Methylene Chloride (mL)	Mass Of Sodium Nitrite (g)	Volume Acetic Acid (mL)	Volume HCl (mL)	Note
JB-2-9	0.96	30	2.02	1.5	0.5	Left overnight, no stirring
JB-2-11	0.96	30	2.03	1.5	0.5	Left for six hours, stirred
JB-2-15a	0.96	30	2.09	1.5	0.5	N_2 sparged, ice bath used, stirred
JB-2-15b	0.96	30	20.15	1.5	0.5	10x amount of sodium nitrite used
JB-2-17a	0.96	0	2.10	1.5	0.5	Water used as reaction medium
JB-2-17b	0.96	0	2.13	6.5	0.5	Acetic acid used as reaction medium
JB-2-17c	0	5	2.10	0	0	Water, benzyl chloride, & benzyl triethylammonium chloride used

Table 3: Variation of parameters for the production of PNM using the method reported by Baruah, et al.

Makosza, et al.[39]also found that the Baruah reaction was erroneous and did not produce the results originally reported.

At this point we began a search for other methods for the direct production of PNM.

In the study of the alkylation of ambident anions, Kornblum reported that under certain conditions, PNM was formed. This reaction proved to be a success and after purification a standard of better than 90% pure PNM was isolated, albeit in low yield. With the isolation of a reliable standard, the focus once again shifted to producing and isolating PNM using the zeolite method.

After the failure to produce the PNM using the Baruah reaction, we attempted to simply produce and isolate enough ourselves for further characterization. While performing these tests, it was decided to use the nitric acid without purifying it because the unpurified acid would have a higher propensity for the nitrogen dioxide.

While re-examining the accumulated data from the aromatic nitration reactions, it was decided to use a zeolite manufactured by Tricat as this zeolite seemed to produce more of the PNM than any of the other zeolite samples. The zeolite used possessed sodium cations rather than acidic protons and is Na-ZSM-5. It was theorized that the Na-ZSM-5 would aid the production of the PNM because the sodium counter ions would not be removed by thermal means (i.e. calcining) and the sodium counter ions would also impede the aromatic substitution by occupying sites that would normally hold acidic protons.

The Tricat zeolite did give better results based simply on the amount of PNM produced per unit of nitrotoluene but the reaction itself was not considered effective since

[39] Makosza, M.,Barbasiewicz, M., Wojciechowski, K. *Synlett* 2001, No.7, 1121-1122.

only a small amount of the PNM was isolated for purification. During this initial testing phase, a method for extracting the PNM from the overall reaction mixture was developed. This method made use of the acidity of the aliphatic protons within the PNM structure, which is relatively high compared to the other, aromatic, protons. The pKa for benzoic acid is 4.20 while the pKa for nitromethane is 10.2 and the pKa for benzaldehyde is greater than 30. By analogy to nitromethane, we expected that NaOH was a strong enough base to enable deprotonation of the PNM. Using a strong base would allow the PNM to be made soluble in water where the nitrotoluenes and benzaldehyde would not be. The PNM could then be removed using simple separatory funnel techniques. The use of the base extraction method was necessary because the PNM boiling point falls in the midst of the nitrotoluenes, making a distillation virtually useless. A few brief attempts at separation using column chromatography had not been successful. The extraction method was proven to be effective even though the overall reaction was not deemed successful due to such a small amount of PNM produced for purification. Earlier data suggested that an increase in the amount of zeolite used might aid in the production of PNM. The use of the DS trap and a reaction performed under reflux was again attempted because of the larger amounts of reactants, specifically the nitric acid volume of 50mL which produced at least 5mL of water, the amount of water in the reaction was significantly increased and it was theorized that this much water might have an even more detrimental effect on the reaction. The reflux reaction does not appear to favor the production of PNM, which is odd in that a higher temperature favors the formation of radicals and thus creates a larger cascade effect. The reflux temperature may have been too high, in effect keeping the radicals from dissolving into the solution and thus

reducing the effects of the radicals on the overall reaction. Another possibility is that the rate of the aromatic substitution increased more than did the radical reaction.

Another test reaction was undertaken using a lower amount of zeolite (25g) and the lower reaction temperature (80-85º C). This combination was found to be the one that produced an appreciable amount of PNM and after purification, a sample of better than 90% was isolated.

After preparing the PNM using the zeolite method, it was characterized and compared with the standard produced using the Kornblum method. The characterization began using the GC chromatograms. The samples of each of the products were prepared in the same manner: 50μL of the product oil was diluted in 1.5mL of dichloromethane; the sample was analyzed using the method given in **Experimental**, GC Analysis Method. The major product has a retention time of 3.178 minutes (See Fig. 27), while the zeolite method product, designated JB-2-71 (See Fig. 28), had a retention time of 3.182 minutes. To further confirm that the two compounds were the same, a mixture of the two products was produced by spiking equal amounts of each product into the same vial and analyzing them together using the same GC method. (See Fig. 29)

This type analysis was considered to be crude at best since any number of materials may elute at those same times, but it was used only as an indication that these two products were close enough in identity to continue characterization analysis. The next type of characterization was the use of proton nuclear magnetic resonance spectrometry, ^{1}H-NMR, to determine if the structure of the two products were of a similar structure.

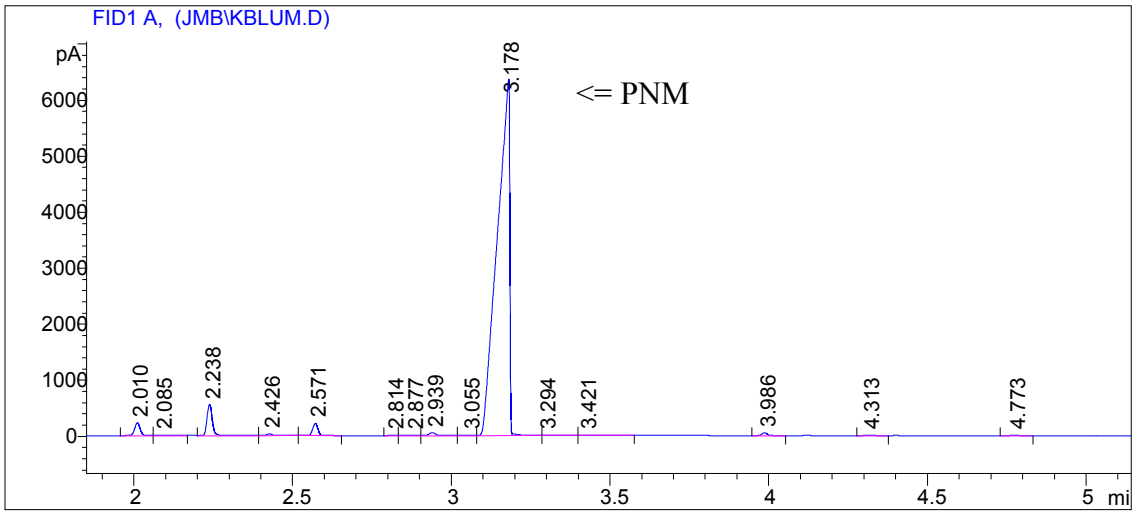


Figure 27: GC chromatogram of the Kornblum product.

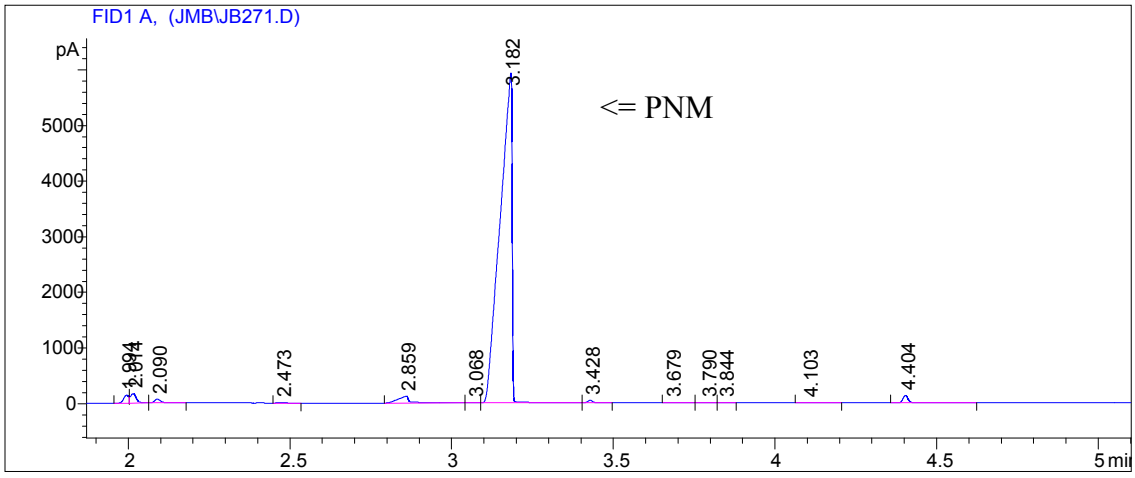


Figure 28: GC chromatogram of JB-2-71.

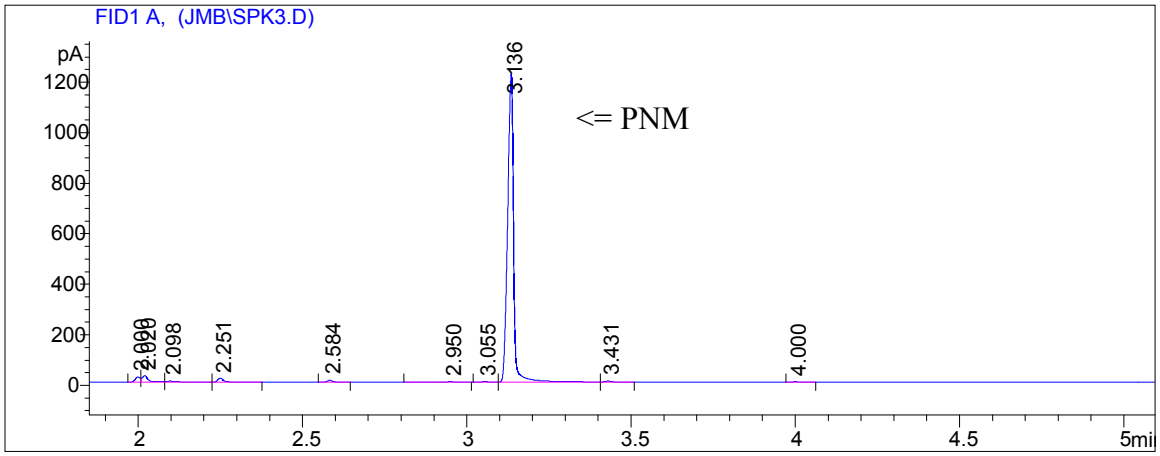


Figure 29: GC chromatogram of Kornblum product and JB-2-71 product spiked.

The ^{1}H-NMR chromatogram (See Fig. 30) shows the product of the Kornblum method with two major peaks at 5.41 ppm, corresponding to the two aliphatic protons, and at 7.42 ppm corresponding to the five aromatic protons. Integration gave a ratio of 5.3:2. The chromatogram of the JB-2-71 product (See Fig. 31) also produces two major signal groups at 5.41 ppm for the two aliphatic protons and 7.42 ppm for the five aromatic protons, respectively, with an integration ratio of 5.3:2. Both of the products are consistent with the 5:2 ratio of aromatic:aliphatic protons expected in PNM. By NMR, the two products are the same as was the case with the GC results. To make the definitive match, a final analysis was performed using infrared spectroscopy (IR), which provided the final piece of data to match the two products as the same compound. The IR analysis was performed based on the transmittance of the material as opposed to the absorbance. Both the Kornblum product and the JB-2-71 product were analyzed using the same method. (See Fig. 32 and Fig. 33, respectively) A composite of the two spectra was created to aid in direct comparison (See Fig. 34), which shows that the two products are virtually identical in all respects and this data taken with the GC and ^{1}H-NMR data, confirm that the two products are in fact that same compound, that of phenylnitromethane, PNM. Table 4 shows all spectrographic data for both the Kornblum product and the JB-2-71 product.

To determine the overall utility of the zeolite method for producing nitrated aliphatics, a series of reactions were undertaken using different materials to be nitrated. The materials chosen were 2,4-dichlorotoluene (DCT) and ethyl benzene and these were chosen because they both possessed an aromatic ring and because each possessed properties different from those of the toluene. The presence of the aromatic ring appears

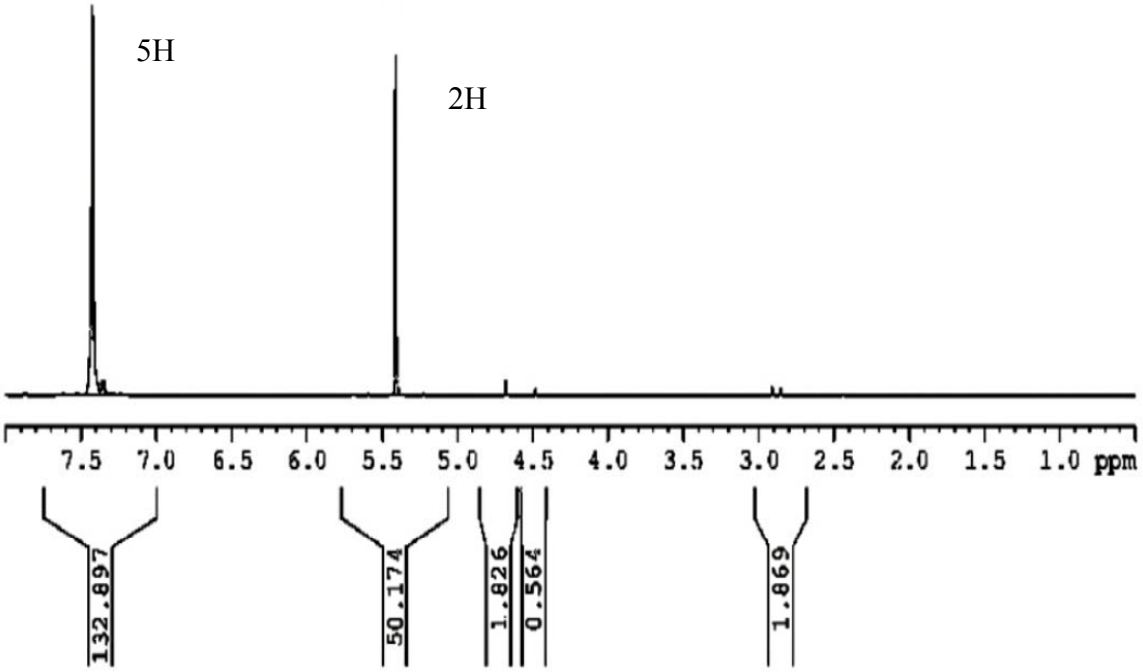


Figure 30: ^{1}H-NMR spectrum of Kornblum product showing 2H at 5.41 ppm and 5H at 7.42 ppm.

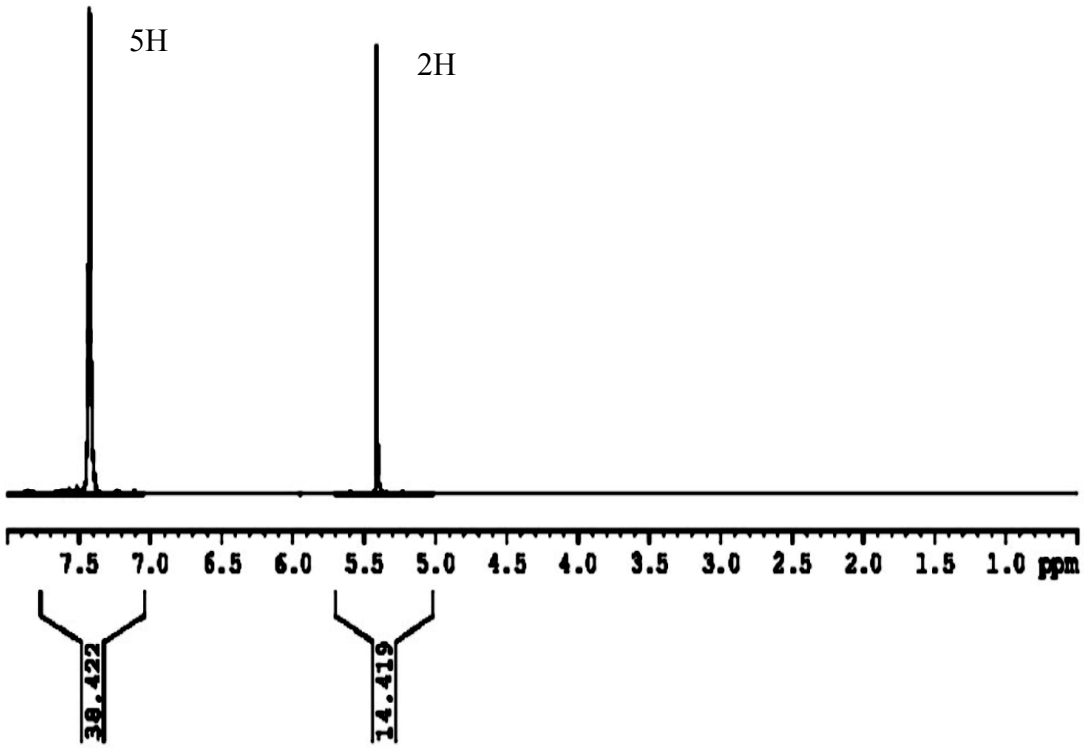


Figure 31: ^{1}H-NMR spectrum of JB-2-71product showing 2H at 5.41 ppm and 5H at 7.42 ppm.

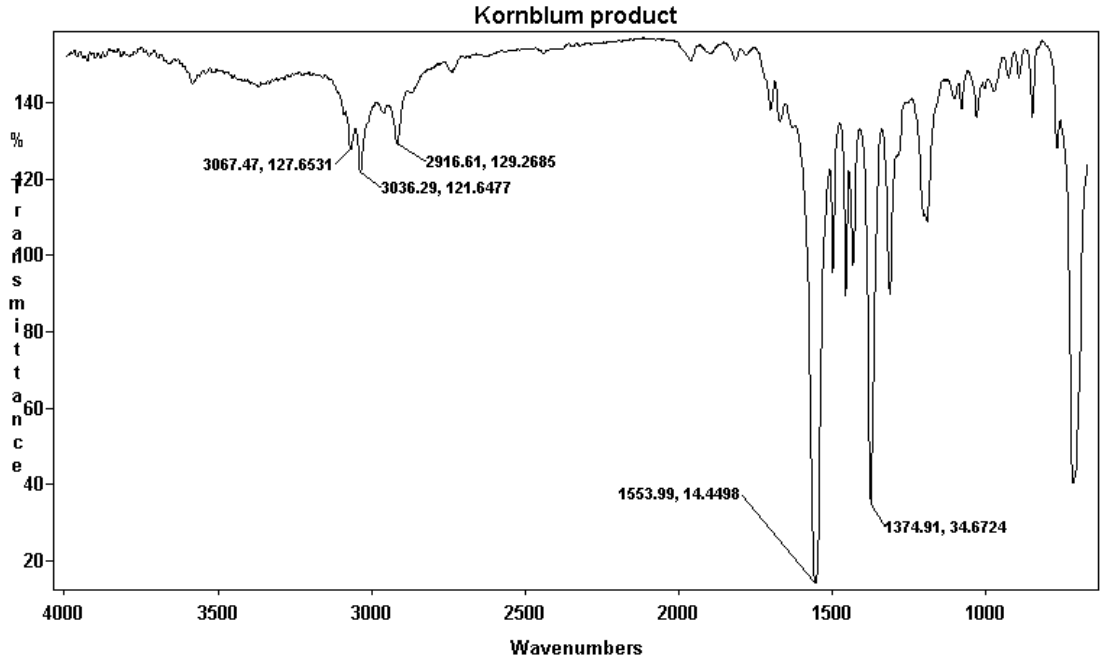


Figure 32: IR spectrum of the Kornblum product.

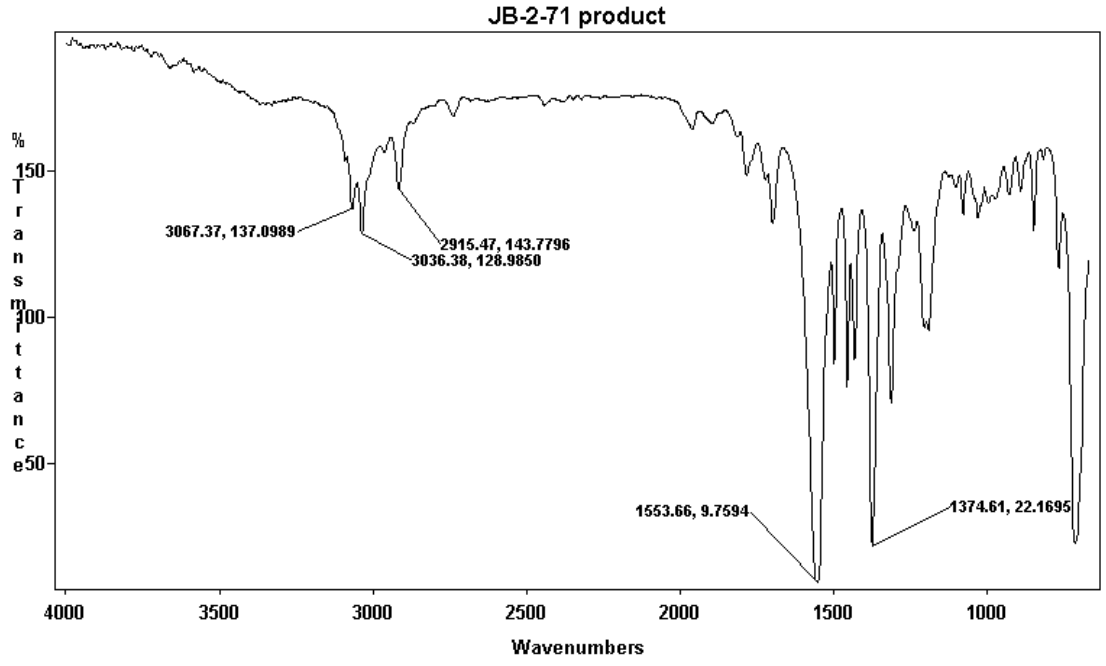


Figure 33: IR spectrum of JB-2-71 product.

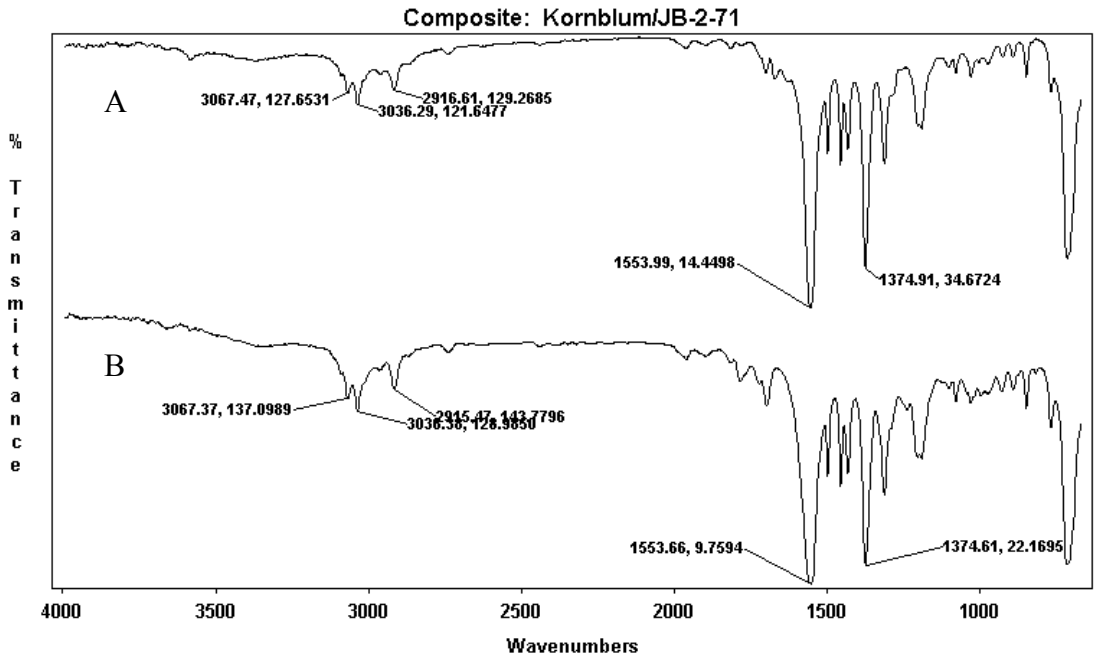


Figure 34: Composite IR spectrum of Kornblum product (A) and JB-2-71 product (B).

		Kornblum product	JB-2-71 product
^{1}H-NMR	2H	5.41 ppm	5.41 ppm
	5H	7.42 ppm	7.42 ppm
IR	Aromatic		
	C-H stretch	3067 cm^{-1}	3067 cm^{-1}
		3036 cm^{-1}	3036 cm^{-1}
	Aliphatic		
	C-H stretch	2916 cm^{-1}	2615 cm^{-1}
	N-O stretch	1554 cm^{-1}	1554 cm^{-1}
GC	Retention time (min)	3.178	3.182

Table 4: Characterization comparison of Kornblum product and JB-2-71 product using ^{1}H-NMR, IR, and GC analyses.

to aid in activating the carbon directly adjacent to the ring for radical addition of the nitro group.

The DCT allowed us to reduce the ring nitration possibilities by the presence of the two chloro-substituents. The addition of the chloro-substituents not only occupied two positions on the aromatic ring but also served to deactivate the ring for electrophilic aromatic substitutions.

While the reaction was successful at nitrating the aliphatic carbon, isolation of the desired product was difficult. The isolation method used involved the use of a base extraction followed by an acidification to retrieve the product, the use of this method allows for the production of 2,4-dichlorobenzaldehyde and 2,4-dichlorobenzoic acid due to the Nef reaction for inserting carbonyl functionality into existing aliphatic systems. Because of the isolation methods used the isolable yields of 2,4-dichlorophenylnitromethane were relatively poor at approximately 2% based on the nitric acid. The isolation and purification methods used exemplified the trouble in removing the desired product in that both produced the benzaldehyde and benzoic acid side products while simultaneously reducing the desired product yields. During the isolation and purification process, the product also showed an unusual affinity for water. After isolation and purification, the product appeared as a waxy yellow solid with a melting range of 57-58º C. GC analysis showed the product to be 95.2% pure (See Fig. 35). A ^{1}H-NMR analysis helped to confirm the structure of the product, (See Fig 36) and an infrared analysis confirmed that the isolated product was the 2,4-dichlorophenylnitromethane showing the characteristic stretches for both the nitro group and aromatic carbons. (See Fig. 37)

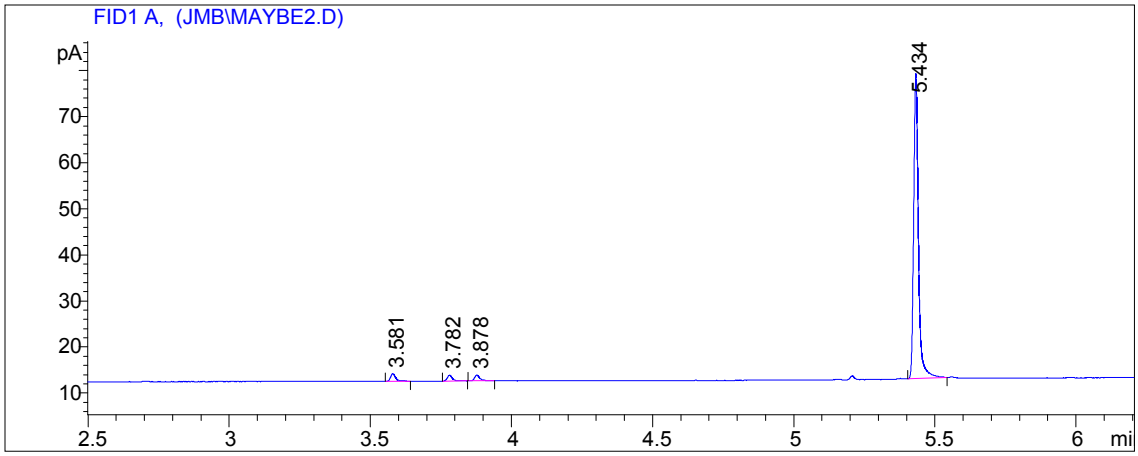


Figure 35: GC chromatogram of 2,4-dichlorophenylnitromethane.

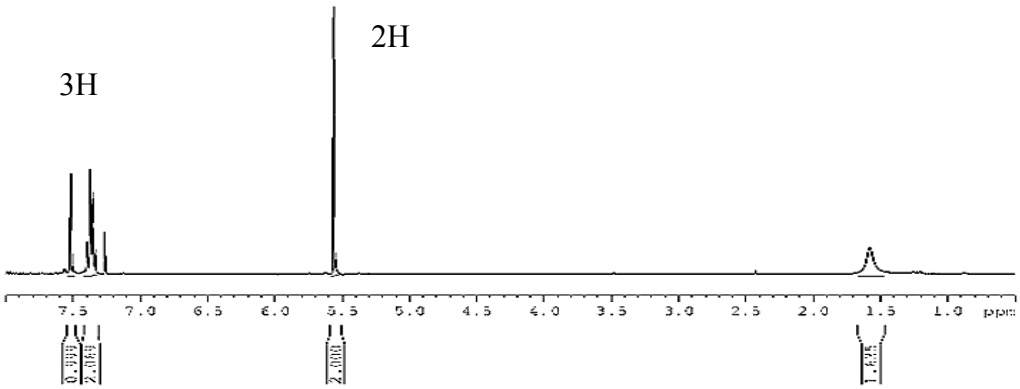


Figure 36: ^{1}H-NMR spectrum of JB-2-101product, 2,4-dichlorophenylnitromethane, showing the aliphatic protons at 5.50 ppm and the aromatic protons at 7.42 and 7.51 ppm (peak at1.6 ppm shown to be water).

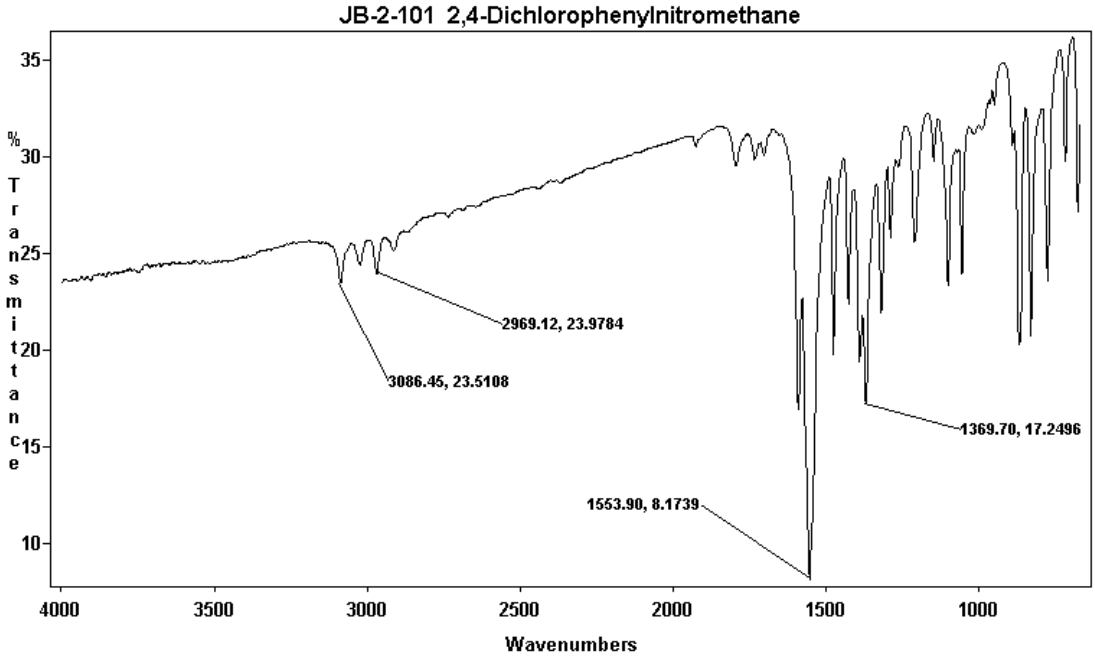


Figure 37: IR spectrum of JB-2-101 product; 2,4-dichlorophenylnitromethane.

The second compound used to test the versatility of the zeolite method for the nitration of aliphatic systems was ethyl benzene. This compound was chosen because of it was similar to the toluene but was different enough to provide a broader picture of the flexibility of the zeolite method. The reaction using the ethyl benzene was the same as that of the toluene and the DCT; this included the isolation and purification methods. The results of the reaction were not as expected, in that we are unsure that the desired product, phenylnitroethane was actually produced. After attempting to isolate the desired product, it was found that we could not remove the compound we thought was the phenylnitroethane from the reaction mixture. After several attempts, using the methods previously established the desired product could not be isolated. The isolation method may have caused the desired product to become a benzaldehyde or benzoic acid derivative but the fact that the desired product could not be extracted from the reaction mixture at all led us to believe that the desired product either had not been formed or was not isolated with the base extraction method used previously. It remains unclear if the desired product was not synthesized or if the extraction technique is unable to remove the desired product from the reaction mixture.

GC analysis of the crude reaction mixture shows the presence of what appeared to be the desired product. (See Fig 38)

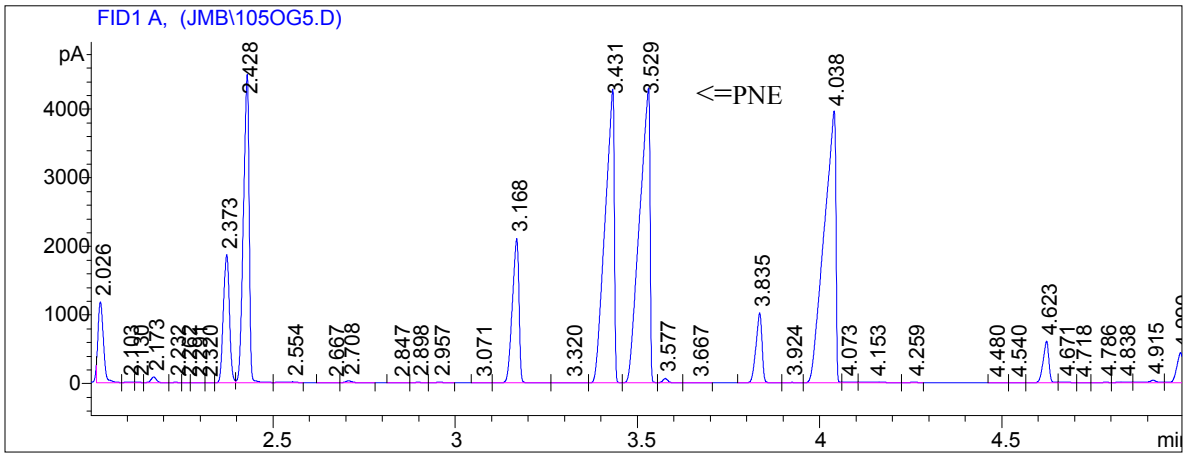


Figure 38: GC chromatogram of phenylnitroethane.

CONCLUSIONS

One study using zeolites and nitric acid reported a considerable increase in the regioselectivity compared to conventional methods. The study reported an isomeric distribution of 17% ortho-, 0.19% meta-, and 83% para-mononitrotoluene with 1.43g.or 43% yield. This study asserted that the regioselectivity of the zeolite reaction was a function of the silica:alumina ratio meaning the reaction could be improved by using zeolites with very high silica:alumina ratios (i.e. 1000 SAR)

Our method using zeolites and nitric acid has produced a comparable isomeric distribution of 17% ortho-, 0.52% meta-, and 83% para-mononitrotoluene. The product yields were approximately half of the original study at 0.73g or 22%. While we could produce comparable isomeric distributions, we found that the regioselectivity was not a function of the silica:alumina ratio. The regioselectivity appears to be more of function of the pore size and the reaction conditions than the silica:alumina ratio.

The production of the ortho- and meta-isomers was found to be the result of an external competing non-zeolite reaction. It was also noted that the nitration reaction would occur under reaction conditions even in the absence of zeolite.

The phenylnitromethane side product was initially considered an impurity to be removed. It was found that not only was the phenylnitromethane not commercially available but there was not a convenient method for producing this compound. The zeolite method can be used to produce not only the phenylnitromethane but also can be used to synthesize other nitrated aliphatics; specifically we synthesized 2,4-dichlorophenylnitromethane, a previously unrecorded compound. The zeolite method offers a new synthetic route to producing nitrated aliphatic compounds.

The reaction for the production of the nitrated aliphatics is thought to be due to a radical mechanism.

REFERENCES

1. Kwok, T.J.; Jayasuriya, K. *J. Org. Chem.* **1994**, *59*, 4939-4942
2. Stock, L.M., "A Classic Mechanism for Aromatic Nitration". *Prog. Phys. Org. Chem.* **1976**, 12, 21-47
3. Waller, F.J.; Barret, A.G.M.; Braddock, D.C.; Ramprasad, D. *Chem. Comm.* **1997**, 613
4. Olah, G.A.; Malhotra, R.; Narang, S.C. *J. Org. Chem.* **1978**, *43*, 4628
5. DeLaude, L.; Laszlo, P.; Smith, K. *Acc. Chem. Res.* **1998**, *26*, 607
6. (a)Laszlo, P. *Acc. Chem. Res.* **1986**, *19*, 121 (b)Laszlo, P.; Vandormael, J. *Chem.Lett.* **1988**, 1843. (c)Cornelis, A.; DeLaude, L.; Gerstmans, A.; Laszlo, P. *Tetrahedron Lett.* **1988**, *29*, 5657
7. Smith, K.;Fry, K; Butters, M.; Nay, B. *Tetrahedron Lett.* **1989**, *30*, 5333
8. Chen, N.Y., et. al. "Molecular transport and reaction in zeolites: design and application of shape selective catalysts." 1994. 15
9. Kucherov, A.V; Slinkin, A.A.; et al. *Catal. Lett.* **1988**, *1*, 311
10. Jayasuriya, K. U.S Patent 5 946 638, 1999
11. Kirk-Othmer Encyclopedia of Chemical Technology. John Wiley & Sons, Inc. New York. 1996. p 204
12. The Nitro Group in Organic Synthesis. Ono, N. Wiley-VCH. New York, 2001. pp. 7
13. Kirk-Othmer Encyclopedia of Chemical Technology. John Wiley & Sons, Inc. New York. 1996. pp 205-207
14. Troops, E.E., Jr. *J. Phys. Chem.* **60**, 304 (1956)
15. Ioffe, S.L., Tartakovskii, V.A., and Novikov, S.S. *Russ. Chem. Rev.* **35**, 19 (1966)
16. The Nitro Group in Organic Synthesis. Ono, N. Wiley-VCH. New York, 2001. pp. 159
17. Noland, W.E., **55**, 137, (1995)
18. Neilsen, A.T., *The Chemistry of Functional Groups; Nitrones, Nitronates, and Nitroxides*, ed. by S. Patai and Z. Rappoport, John Wiley, London, 1989
19. Pinnick, H.W. In *Organic Reacitons*, ed. by L.A. Paquette, John Wiley, **38**, Chapter 3 (1990)
20. The Nitro Group in Organic Synthesis. Ono, N. Wiley-VCH. New York, 2001. pp. 160
21. Shechter, H., and Williams,F.T. *J. Org. Chem* .**27,** 369 (1962)
22. Olah, G.A., Aravananaghi, M., Vankar, Y.D., Prakash, G.K.S. *Synthesis*, 662 (1980)
23. McMurry, J.E., Melton, J., Padgett, H. *J. Org. Chem.* **39**, 259 (1974); *Org. Synth*. **6**, 648 (1988)
24. Ballini, E., Petrini, M. *Tetrahedron Lett*., **30**, 5329 (1989)
25. The Nitro Group in Organic Synthesis. Ono, N. Wiley-VCH. New York, 2001. pp. 161
26. McMurry, J.E., Melton, J. *J. Am. Chem. Soc.* **93**, 5309 (1971)
27. McMurry, J.E., Melton, J. *J. Org. Chem.*, **38**, 4367 (1973)
28. The Nitro Group in Organic Synthesis. Ono, N. Wiley-VCH. New York, 2001. pp. 165
29. Kornblum, N., Weaver, W., *J. Am. Chem. Soc.* **80**, 4333 (1958)

30. Vollhardt and Schore, 2nd Edition Chapters 21, 22 and 26
31. ibid.
32. ibid
33. V. Meyer, Ann. 1874, 171, p. 1 et seq.
34. Bamberger, Schmidt, and Levinson, ibid. **33**, 2053 (1900)
35. Hollemann, Rec. trav. Chim. **13**, 403 (1894)
36. Hantzsch, and Schultze, Ber. **29**, 700 (1896)
37. Wislicenus and Endres, ibid. **35**, 1755 (1902); cf. Gatterman-Weiland, "Laboratory Methods of Organic Chemistry," p. 256. Translated from the twenty-fourth German edition by W. McCartney, the MacMillan Company, New York, 1937
38. Baruah, A., Kalita, B., Barua, C. *Synlett*. **7**, 1064-1065 (2000)
39. Makosza, M., Barbasiewicz, M., Wojciechowski, K. *Synlett.* **2001**, 7, 1121-1122
40. Freeman, P., Shepard, I.G. *Org. Syn.,* **43**, 84 (1963)
41. Peng, X., Suzuki, H., Lu, C. *Tetrahedron Letters*. **42**, 4357-4359 (2001)
42. Babers, F., Black, A. *Org. Syn.* CV 2, 512

APPENDIX

Appendix A. Raw data for GC detector correction factor.

50 micro	stock mL	area dec	area o	area m	area p	total area NT	Area NT/Area Dec	(mL dec)/Area NT/area Dec	g nT	Calculated from Eq.1	%o	%m	%p
0.05	0.1	674	70	6	163	239	0.355	0.018	0.02	1.128	29.3	2.5	68.2
0.05	0.2	621	137	11	322	470	0.757	0.038	0.04	1.057	29.1	2.3	68.5
0.05	0.4	654	287	23	672	982	1.502	0.075	0.08	1.066	29.2	2.3	68.4
0.05	1	629	706	57	1662	2425	3.855	0.193	0.2	1.038	29.1	2.4	68.5
0.05	2	615	1389	113	3273	4775	7.764	0.388	0.4	1.030	29.1	2.4	68.5
0.05	3	601	2112	173	4975	7260	12.080	0.604	0.6	0.993	29.1	2.4	68.5
									Aver	1.052			

200 micro	stock mL	area dec	area o	area m	area p	total area NT	Area NT/Area Dec	(mL dec)/Area NT/area Dec	g nT	Calculated from Eq.1	%o	%m	%p
0.2	0.1	2368	72	6	168	246	0.104	0.021	0.02	0.963	29.3	2.4	68.3
0.2	0.2	2497	142	11	331	484	0.194	0.039	0.04	1.032	29.3	2.3	68.4
0.2	0.4	2409	278	22	652	952	0.395	0.079	0.08	1.012	29.2	2.3	68.5
0.2	1	2484	724	59	1702	2485	1.000	0.200	0.2	1.000	29.1	2.4	68.5
0.2	2	2418	1395	114	3284	4793	1.982	0.396	0.4	1.009	29.1	2.4	68.5
0.2	3	2550	2166	177	5103	7446	2.920	0.584	0.6	1.027	29.1	2.4	68.5
									Aver	1.007			

Vol Dec	stock mL	area dec	area o	area m	area p	total area NT	Area NT/Area Dec	(mL dec)Area NT/area Dec	g nT	factor	%o	%m	%p
0.025	0.2	395	146	12	342	500	1.266	0.032	0.04	1.264	28.2	2.4	68.4
0.05	0.2	667	150	12	352	514	0.771	0.039	0.04	1.038	28.2	2.3	68.5
0.1	0.2	1282	147	12	345	504	0.390	0.039	0.04	1.025	28.2	2.4	68.5
0.2	0.2	2474	145	12	339	496	0.200	0.040	0.04	0.998	28.2	2.4	68.3
0.5	0.2	6192	149	11	336	490	0.079	0.040	0.04	1.011	28.2	2.2	68.6
										Average	1.027		

Appendix B: Master reference chart for aromatic nitration reactions.

NB # JB1-	SAR	Zeolite (g)/100 mL Toluene	mL HNO_3/ 100 mL Toluene	o:m:p ratio (%)	Total NT yield; **%** (end of Rxn)	Total PNM yield; **%** (end of Rxn)	Area NT/ Area PNM (end of Rxn)	Z:T Ratio	Comment
3	280	12.5	1.23	21.3: 1.5: 76.9	38.3	38.0	1	1:8	Air 305 oven.
6	280	12.5	1.5	17.3: 1.5: 81.3	46.7	31.4	1*	1:8	Evaporation issues (no grease on joints) 305 oven.
11	280	12.56	2.25	22.2: 1.5: 76.3	30.4	23.7	1	1:8	Magnetic stirrer. 305 oven.
13	280	12.56	2.25	31.6: 1.9: 72.8	27.3	6.88	4	1:8	Reduced temp (room ≈25° C) 305 oven.
17	280	25.0	2.25	25.2: 1.9: 72.8	53.3	18.4	3	1:4	Zeolite amt. Increased. 305 oven.
19	280	50.0	2.25	30.9: 2.4: 66.7	157.8	8.89	15*	1:2	Evaporation issues. 305 oven.
43	280	50.08	2.25	36.2: 3.1: 60.8	97.8	3.60	27	1:2	305 oven.
45	280	50.08	2.25	33.0: 2.9: 64.2	94.6	5.76	16	1:2	Reduced temp (65-70° C). 305 oven.
47	280	50.04	2.25	33.5: 2.9: 63.6	81.9	9.35	9	1:2	Slow add HNO_3. 305 oven.
49	1000	50.04	2.25	27.1:2.54:70.4	59.7	28.2	2	1:2	Rxn using ratio 1000 zeolite. 305 oven.

51	80	38.3	2.25	29.6:1.61:68.8	114	5.32	21*	1:2.6	Rxn using ratio 80 zeolite. Liquid parameters increased by 30 % due to absorption of toluene by zeolite. 305 oven.
53	250-300	50.1	2.25	24.6:2.09:73.3	173	53.7	3*	1:2	Rxn using Tricat zeolite normal soda levels ratio 250-300. Little absorption of toluene by zeolite, mix is very thin.. 305 oven.
55	250-300	50	2.25	20.5:1.59:77.9	86.9	7.48	11	1:2	Rxn using Tricat zeolite low soda level ratio 250-300. Mix is thin gel. 305 oven.
57	1000	50.28	2.25	43.7:4.13:52.2	42.1	64.4	0.7	1:2	Rxn using Tricat calcined @ 550 C for 2 hrs ratio 1000. Mix colored from white/gray to dark orange and back. 550 oven.

25	1000	50	2.26	16.7:1.47:81.8	No Data.	33.7	Na	1:4	No decane used. Mulitple nitric add. 550 oven.
59	1000	50.6	2.25	20.8:2.19:77.0	34.1	48.5	0.7	1:2	Rxn using Tricat pelletized ratio 1000. Stirring problems. 550 oven.
61	280	25.47	2.25	19.1:0.78:80.1	78.2	4.58	17	1:4	Nitrogen sweep added to rxn in an effort to remove Di-nitrogen tetroxide. 305 oven.
63	280	25.08	2.25	18.8:0.89:80.3	71.3	1.95	37	1:4	Nitrogen sweep & reflux. Used DS Trap to remove water. ? oven.
65	280	25.43	2.25	22.8:1.06:76.1	82.4	6.83	12	1:4	N_2 sparge. Low temp init; high to end. 305 oven.
67	1000	25.40	2.25	24.4:2.24:73.3	62.8	1.20	52	1:4	Repeat of 63 with 1000. 305 oven. N_2 sparge.
69	80	25.22	2.25	31.9:2.38:65.7	63.9	0	0	1:4	Repeat of 63 with 80. 305 oven. N_2 sparge.

71	280	25.27	2.25	53.7:5.07:41.2	232.7	0.37	623*	1:4	Repeat 17; added H_2SO_4 before nitric. 305 oven.
73	80	33.43	2.23	No Data.	No Data.	No Data.	Na	1:3	Rxn terminated early due to "explosive" bump. 305 oven.
75	80	33.31	2.23	35.7:2.94:61.3	53.4	0	0	1:3	Repeat of 63. Mix left overnight. 305 oven. N_2 sparge.
77	1000	33.36	2.23	23.4:2.14:74.4	62.4	2.08	30	1:3	305 oven. N_2 sparge.
79	280	33.29	2.23	28.9:2.19:68.9	68.1	0.04	1647	1:3	305 oven. N_2 sparge.
81	80	20.3	2.2	28.1:2.48:69.5	70.0	0	0	1:5	305 oven. N_2 sparge.
83	1000	20.5	22.5	54.8:4.93:40.2	31.5	0	0	2:1	Hexane used as medium. 305 oven.
99	80	20.01	2.2	No Data.	No Data.	No Data.	Na	1:5	No fractions taken. Real yields determined. ? oven.
105	80	20.27	2.2	35.7:3.50:60.8	27.2	0.08	333	1:5	TEOS used. 550 oven.
107	30	20.04	2.2	33.6:3.36:63.0	56.3	0.81	69	1:5	550 oven.
109	280	20.21	2.2	41.1:3.89:55.0	48.0	2.48	19	1:5	550 oven. Top charge w/ nitric.

113	280	25.43	2.2	17.7:1.03:81.25	58.9	19.1	3	1:4	Clean nitric. No N_2; sparge or pad. Under air. No reflux. Reference 17. 550 oven.
115	280	20.10	2.2	21.9:1.52:76.6	71.6	1.33	54	1:5	Clean nitric. 550 oven. N_2 sparge.
117	280	25.12	2.2	19.8:1.03:79.2	101.1	2.12	48	1:4	Clean nitric. Normal temp 90-95 C. 550 oven. N_2 sparge.
119	280	25.12	2.2	28.8:2.10:69.1	92.2	0.57	161	1:4	Clean nitric. Acetic anhydride used. 550 oven. N_2 sparge.
121	280	25.06	2.2	21.1:1.34:77.5	79.8	1.78	45	1:4	Clean nitric. Cool temp 80-85 C. 550 oven. N_2 sparge.
123	Exp	25.14	2.2	53.3:3.96:42.7	34.1	0.11	303	1:4	Clean nitric. Cool temp 80-85 C. 550 oven. **G-ZSM-5 Catalyst C** N_2 sparge.
125	Exp	25.66	2.2	50.9:3.90:45.1	27.7	0.37	75	1:4	Clean nitric. Cool temp 80-85 C. 550 oven. **G-ZSM-5 Catalyst A** N_2 sparge.

127	Exp	25.11	2.2	53.3:4.92:41.8	3.12	0	0	1:4	Clean nitric. Cool temp 80-85 C. 550 oven. **FMC Fovet Zeolite 4A** N_2 sparge.
129	Exp	25.4	2.2	53.5:5.19:41.5	5.68	0	0	1:4	Clean nitric. Cool temp 80-85 C. 550 oven. **Albamarle EZA Catalyst A** N_2 sparge.
131	Exp	25.16	2.2	32.8:2.58:64.6	55.4	0.38	145	1:4	Clean nitric. Cool temp 80-85 C. 550 oven. **G-Zeolite-Z1** N_2 sparge.
133	Exp	25.1	2.2	29.5:2.43:68.1	44.9	1.32	34	1:4	Clean nitric. Cool temp 80-85 C. 550 oven. **G-Zeolite-Z2** N_2 sparge.
135	Exp	25.06	2.2	52.9:3.10:44.0	7.55	0	0	1:4	Clean nitric. Cool temp 80-85 C. 550 oven. **G-Zeolite-Z3** N_2 sparge.
137	Exp	25.2	2.2	52.8:2.84:44.4	23.0	0	0	1:4	Clean nitric. Cool temp 80-85 C. 550 oven. **G-Zeolite-Z4** N_2 sparge.
139	280	25.04	2.2	18.9:0.81:80.3	87.4	1.36	64	1:4	Clean nitric. Cool temp 80-85 C. 550 oven. N_2 sparge.

141	Exp	25.1	2.2	53.4:4.12:42.5	34.7	0.13	261	1:4	Clean nitric. Cool temp 80-85 C. 550 oven. **G-ZSM-5 Catalyst B** N_2 sparge.
143	N/a	N/a	2.2	56.4:5.37:38.2	15.9	0.05	335	N/a	Clean nitric. No zeolite. Cool temp. N_2 sparge.
145	280	25.2	2.8	15.1:0.77:84.1	66.5	0.70	95	1:4	Conc Nitric (70%). Cool temp. 80-85 C. 550 oven. N_2 sparge.
147	N/a	N/a	2.2	55.6:5.07:39.4	9.54	0.05	207	N/a	Clean nitric. No zeolite. Cool temp. No N_2 sparge or pad.
149	280	25	2.2	22.4:2.53:75.1	18.2	11.0	2	1:4	Clean nitric. 90-95 C. No N_2 sparge or pad. BHT used. 550 oven.
151	280	25.01	2.2	18.5:1.37:80.1	56.2	3.48	16	1:4	Clean nitric. 80-85 C. N_2 sparge. BHT used. 550 oven.

NB # JB2-	SAR	Zeolite (g)/100 mL Toluene	mL HNO_3/ 100 mL Toluene	o:m:p ratio (%)	Total N-T yield; **%** (end of Rxn)	Total PNM yield; **%** (end of Rxn)	Area NT/ Area PNM (end of Rxn)	Z:T Ratio	Comment
1	280	25.2	2.2	21.3:0.41:78.3	59.8	0.35		1:4	Clean nitric. CH_3Cl used for pre-treat of nitric to zeo. N_2 sparge. 78 C. 550 oven.
5	280	25	2.2	16.6:0.52:82.8	17.6	0.55		1:4	Repeat of JB2-1. Some zeo made it through filter.